Fibers Bibliography, with Abstracts
Key to Numeric Codes

Asbestos-related, non-cancer (health/irritant effects, metabolism, mechanisms)
1– smaller than 5 microns
2– larger than 5 microns
3– size not specified

Asbestos-related, cancer (health/irritant effects, metabolism, mechanisms)
4– smaller than 5 microns
5– larger than 5 microns
6– size not specified

Asbestos-related, non-cancer and cancer (health/irritant effects, metabolism, mechanisms)
1, 2, 3, 4, 5, 6

Asbestos and Man-made Vitreous Fibers (MMVFs), pulmonary depositional patterns, biopersistence, miscellaneous of potential relevance
7

Man-made Vitreous Fibers (MMVFs), non-cancer (health/irritant effects, metabolism, mechanisms)
8– MMVFs
10– fiberglass

Man-made Vitreous Fibers (MMVFs), cancer (health/irritant effects, metabolism, mechanisms)
9– MMVFs
10– fiberglass

Man-made Vitreous Fibers (MMVFs), non-cancer and cancer (health/irritant effects, metabolism, mechanisms)
8, 9, 10

Asbestos and Man-made Vitreous Fibers (MMVFs), non-cancer (health/irritant effects, metabolism, mechanisms)
1, 2, 3, 8, 10

Asbestos and Man-made Vitreous Fibers (MMVFs), cancer (health/irritant effects, metabolism, mechanisms)
4, 5, 6, 9, 10

Man-made Vitreous Fibers, exposures (exposure levels, fiber size, no health effects)
11

Review Papers
14– asbestos
15– MMVFs

Unknown Relevance
90

Fibers Bibliography, with Abstracts

Asbestos-related, non-cancer (1, 2, 3)
—health/irritant effects, metabolism, mechanisms

Code(s): 1.
Haque, A. K., D. M. Vrazel, K. D. Burau, S. P. Cooper and T. Downs. (1996). "Is there transplacental transfer of asbestos? A study of 40 stillborn infants." Pediatr Pathol Lab Med. 16 (6): 877-92.
An autopsy study was conducted to investigate whether there is transplacental transfer of asbestos in humans. The asbestos burden of lung, liver, skeletal muscle, and placenta digests of 40 stillborn infants was determined using a bleach digestion method. The fibers detected in the tissue digests were characterized as to the type of asbestos, using electron microscopy, energy-dispersive x-ray analysis, and selected-area diffraction analysis. Placental digests of 45 full- term, liveborn infants were similarly processed as controls. Low levels of small, thin, uncoated asbestos fibers were detected in the placentas and organs of 37.5% of the stillborn infants (15 of 40). The fiber sizes ranged from 0.05 to 5.0 microns in length and 0.03 to 0.3 micron in width, with a mean length of 1.15 microns and a mean width of 0.069 micron. Maximum numbers of fibers were found in the lungs (mean 235,400 fibers/g; n = 10), followed by liver (mean 212,833 fibers/g; n = 6), placenta (mean 164,500 fibers/g; n = 4), and skeletal muscle (80,000 fibers/g; n = 1). The fibers were detected at all stages of gestation and showed no association with gestational age. A significant association was found between fiber presence and working mothers, and positive but nonsignificant associations were found with maternal history of drug abuse, previous abortions, and fetal maceration. No association was found between premature rupture of membranes and fiber presence. No fibers were detected in the 45 placentas of the liveborn control infants. There was a highly significant difference in the asbestos fiber counts of the placentas of the stillborn and liveborn infants ($P < .001$). Our studies demonstrate the presence of short and thin asbestos fibers in stillborn infants and their positive association with working mothers.

Code(s): 1, 2.
Dufresne, A., R. Begin, A. Churg and S. Masse. (1996). "Mineral fiber content of lungs in patients with mesothelioma seeking compensation in Quebec." Am J Respir Crit Care Med. 153 (2): 711-8.
Asbestos fibers (AF) and ferruginous bodies (FB) in lung parenchyma from 50 workers seeking compensation from the Workers' Compensation Board of Quebec for pleural or peritoneal mesothelioma were analyzed using transmission electron microscopy (TEM) equipped with energy- dispersive spectrometer (EDS) and phase-contrast microscopy (PCM). These workers had been occupationally exposed in mining and milling activities (12 were from Asbestos Township and 11 from Thetford Mines) and 27 were from other types of industry (asbestos factory, shipyard, etc.). For comparison, analyses of lung tissue at autopsy were done in a group of 49 subjects from a reference population. A 95% confidence interval upper limit of 540 AF < 5 microns/mg and a 95% confidence interval upper limit of 161 AF > or = 5 microns/mg dried lung tissue were found for the reference population. Similarly, a concentration of FB of 142 FB/g constituted the upper limit of detectable FB in the lungs of the reference population. Forty-eight of the 50 workers with mesothelioma had either a ferruginous body or total asbestos fiber count greater than the 95% confidence interval for the reference population; the remaining two had amosite and/or crocidolite concentrations greater than the 95% confidence interval for the reference population. The fiber types were different in the three groups, with the lungs of workers from Thetford Mines containing only chrysotile and tremolite, those from Asbestos Township containing chrysotile, tremolite, amosite, and crocidolite, and those in other industries containing largely amosite and crocidolite. We conclude that in this population of workers seeking compensation for mesothelioma, fiber analysis confirmed occupational asbestos exposure in every case. The fiber types responsible for the tumors are probably different in the three different groups.

Code(s): 1, 2, 4, 5.
Dufresne, A., R. Begin, S. Masse, C. M. Dufresne, P. Loosereewanich and G. Perrault. (1996). "Retention of asbestos fibres in lungs of workers with asbestosis, asbestosis and lung cancer, and mesothelioma in Asbestos township." Occup Environ Med. 53 (12): 801-7.
OBJECTIVE: To conduct a mineralogical study on the particles retained in the necropsied lungs of a homogenous group of asbestos miners and millers from Asbestos township (and a local reference population) and to consider the hypothesis that there is a difference in size between fibres retained in the lungs of patients with asbestosis with and without lung cancer. METHODS: Samples of lung tissue were obtained from 38 patients with asbestosis without lung cancer, 25 with asbestosis and lung cancer, and 12 with mesothelioma, from necropsied Quebec chrysotile miners and millers from Asbestos township. Fibre concentrations in the lungs of these patients were compared with those in tissue from necropsies carried out on a local reference population: men who had died of either accidental death or acute myocardial infarction between 1990 and 1992. 23 were born before 1940 and 26 after 1940. RESULTS: Geometric mean (GM) concentrations were higher in cases than in the controls for chrysotile fibres 5 to 10 microns long in patients with asbestosis with or without lung cancer; for tremolite fibres 5 to 10 microns long in all patients; for crocidolite, talc, or anthophyllite fibres 5 to 10 microns long in patients with mesothelioma; for chrysotile and tremolite fibres > or = 10 microns long in patients with asbestosis; and crocidolite, talc, or anthophyllite fibres > or = 10 microns long in patients with mesothelioma. However,

median concentrations of each type of fibre in the lungs did not show any significant differences between the three disease groups. Average length to diameter ratios of the fibres were calculated to be larger in patients with asbestosis and lung cancer than in those without lung cancer for crocidolite fibres > or = 10 microns long, for chrysotile, amosite, and tremolite fibres 5 to 10 microns long, and for chrysotile and crocidolite fibres < 5 microns long. However, there was no statistical difference in the median length to diameter ratios for any type of fibres across the disease groups when they were calculated in each patient. Cumulative smoking index (pack-years) was higher in the group with asbestosis and lung cancer but was not statistically different from the two other disease groups. CONCLUSION: Lung cancers occurred in workers with asbestosis from Asbestos township who had an equal concentration of retained fibres but a tendency to a higher length to diameter ratio of amphiboles. These workers had a 29% higher average cumulative smoking index.

Code(s): 1, 2, 7.
Finkelstein, M. M. and A. Dufresne. (1999). "Inferences on the kinetics of asbestos deposition and clearance among chrysotile miners and millers." Am J Ind Med. 35 (4): 401-12.
BACKGROUND: The health effects of asbestos are intimately related to the fate of inhaled fibers in the lungs. The kinetics of asbestos fibers have been studied primarily in rodents. The objective of this study was to explore the application of these kinetic models to human autopsy data. METHODS: We analyzed the asbestos fiber content of the lungs of 72 Quebec chrysotile miners and millers and 49 control subjects using analytical transmission electron microscopy. Statistical methods included standard multivariate linear regression and locally weighted regression methods. RESULTS: The lung burdens of asbestos bodies and chrysotile and tremolite fibers were correlated, as were the concentrations of short, medium, and long fibers of each asbestos variety. There were significant associations between the duration of occupational exposure and the burdens of chrysotile and tremolite. The concentration of chrysotile decreased with the time since last exposure but the concentration of tremolite did not. The clearance rate varied inversely with the length of chrysotile fibers. For fibers greater than 10 mu in length the clearance half-time was estimated to be 8 years. CONCLUSIONS: The patterns in our data are compatible with both of the hypotheses suggested from rodent experiments; the existence of a long- term sequestration compartment and overload of clearance mechanisms in this compartment.

Code(s): 1, 2, 11.
Murai, Y., M. Kitagawa and T. Hiraoka. (1995). "Asbestos body formation in the human lung: distinctions, by type and size." Arch Environ Health. 50 (1): 19-25.
The fraction of fibers coated in a total of 3,800 asbestos fibers from 38 patients with disease related to asbestos (100 fibers per patient) was determined, according to asbestos fiber type and size parameters. Among the 3,800 fibers, 638 (16.8%) were coated and 3,162 were uncoated. All fibers were analyzed at 2,000 x magnification (lower limit of detection: 2 microns for length and 0.06 microns for diameter). The diameter of the totally coated fibers (28.4% of total bodies; 181/638) was not measured. The percentage of coated fibers varied with the asbestos type; it was 27.1% (335/1235) for amosite fibers, 16.0% (228/1423) for crocidolite, 6.6% (60/908) for tremolite or actinolite, 6.5% (14/214) for anthophyllite, and 5% (1/20) for chrysotile fibers. Most coated fibers were longer than 10 microns and had an aspect ratio (length/diameter) of more than 20. Approximately 60% of coated fibers had an aspect ratio of more than 100. The longer the fiber, the greater the percentage of coated fibers, regardless of diameter. The increase in the percentage associated with length was more marked in fibers with a smaller diameter; the percentage of coated fibers was, therefore, greater in fibers 30 microns or less in diameter. However, in fibers longer than 30 microns, the relationship to percentage of coated fibers was not as clear, and the diameter was less important. Accordingly, the fibers with high aspect ratios, particularly long fibers, tended to show asbestos body formation. The percentage of long fibers was highest in amosite, and the percentage of fibers with an aspect ratio of more than 100 was highest in amosite and crocidolite.(ABSTRACT TRUNCATED AT 250 WORDS)

Code(s): 2.
Pache, J. C., Y. M. Janssen, E. S. Walsh, T. R. Quinlan, C. L. Zanella, R. B. Low, D. J. Taatjes and B. T. Mossman. (1998). "Increased epidermal growth factor-receptor protein in a human mesothelial cell line in response to long asbestos fibers." Am J Pathol. 152 (2): 333-40.
Epidermal growth factor (EGF) is a potent mitogen for human mesothelial cells, and autophosphorylation of the EGF receptor (EGF-R) occurs in these cell types after exposure to asbestos, a carcinogen associated with the development of mesothelioma. Here, the intensity and distribution of EGF-R protein was documented by immunocytochemistry in a human mesothelial cell line (MET5A) exposed to various concentrations of crocidolite asbestos and man-made vitreous fibers (MMVF-10). Whereas cells in contact with or phagocytizing shorter asbestos fibers (<60 microm length) or MMVF-10 at a range of concentrations showed no increase in EGF-R protein as determined by immunofluorescence, elongated cells phagocytizing and surrounding longer fibers (> or =60 microm) showed intense staining for EGF-R. In contrast, human A549 lung carcinoma cells showed neither elongation nor increased accumulation of EGF-R protein in response to long fibers. Patterns of aggregation and increases in EGF-R protein in mesothelial cells phagocytizing long asbestos fibers were distinct from diffuse staining of phosphotyrosine residues observed in asbestos-exposed cultures. These studies indicate that aggregation of EGF-R by long fibers may initiate cell signaling cascades important in asbestos-induced

mitogenesis and carcinogenesis.

Code(s): 2.
Boutin, C., P. Dumortier, F. Rey, J. R. Viallat and P. De Vuyst. (1996). "Black spots concentrate oncogenic asbestos fibers in the parietal pleura. Thoracoscopic and mineralogic study." Am J Respir Crit Care Med. 153 (1): 444-9.
Epidemiologic and pathologic data demonstrate that malignant mesothelioma occurs preferentially after exposure to long amphibole asbestos fibers. However, mineralogic studies have rarely detected such fibers in the parietal pleura. We hypothesized that the distribution of asbestos fibers in the pleura was heterogeneous and that they might concentrate in certain areas, as does coal dust in patients showing anthracotic "black spots" of the parietal pleura during thoracoscopy. We collected thoracoscopic biopsy samples from these black spots and from normal areas of the parietal pleura and lung from 14 subjects (eight with and six without asbestos exposure). Asbestos content was determined by transmission electron microscopy. In exposed subjects, mean fiber concentrations were 12.4 +/- 9.8 x 10(6) fibers/g of dry tissue in lung, 4.1 +/- 1.9 in black spots, and 0.5 +/- 0.2 in normal pleura. In unexposed patients, concentrations were 0, 0.3 +/- 0.1, and 0, respectively. Amphiboles outnumbered chrysotile in all samples. A total of 22.5% of fibers were > or = 5 microns in length in black spots. A histologic similarity of these black spots with milky spots is suggested by conventional and electron microscopy. We conclude that the distribution of asbestos fibers is heterogeneous in the parietal pleura. Indeed, the fibers concentrate in black spots, where they can reach high concentrations. These findings could explain why the parietal pleura is the target organ for mesothelioma and plaques.

Code(s): 2.
Dufresne, A., M. Harrigan, S. Masse and R. Begin. (1995). "Fibers in lung tissues of mesothelioma cases among miners and millers of the township of Asbestos, Quebec." Am J Ind Med. 27 (4): 581-92.
Twenty cases of mesothelioma among miners of the township of Asbestos, Quebec, Canada, have been reported. To further explore the mineral characteristics of various fibrous material, we studied the fibrous inorganic content of postmortem lung tissues of 12 of 20 available cases. In each case, we measured concentrations of chrysotile, amosite, crocidolite, tremolite, talc-anthophyllite, and other fibrous minerals. The average diameter, length, and length-to-diameter ratio of each type of fiber were also calculated. For total fibers > 5 microns, we found > 1,000 asbestos fibers per mg tissue (f/mg) in all cases; tremolite was above 1,000 f/mg in 8 cases, chrysotile in 6 cases, crocidolite in 4 cases, and talc anthophyllite in 5 cases. Among cases with asbestos fibers, the tremolite count was highest in 7 cases, chrysotile in 3 cases, and crocidolite in 2 cases. The geometric mean concentrations of fibers > or = 5 microns were in the following decreasing order: tremolite > crocidolite > chrysotile > other fibers > talc- anthophyllite > amosite. For total fibers < 5 microns, we found > 1,000 fibers per mg tissue (f/mg) in all cases; tremolite was above 1,000 f/mg in 12 cases, chrysotile in 8 cases, crocidolite in 7 cases, and talc-anthophyllite in 6 cases. Tremolite was highest in 8 cases, chrysotile in 2 cases, and crocidolite and amosite in 2 cases. The geometric mean concentrations of fibers < 5 microns were in the following decreasing order: tremolite > other fibers > chrysotile > crocidolite > talc-anthophyllite > amosite. We conclude, on the basis of the lung burden analyses of 12 mesothelioma cases from the Asbestos township of Quebec, that the imported amphibole (crocidolite and amosite) were the dominant fibers retained in the lung tissue in 2/12 cases. In 10/12 cases, fibers from the mine site (chrysotile and tremolite) were found at highest counts; tremolite was clearly the highest in 6, chrysotile in 2, and 2 cases had about the same counts for tremolite and chrysotile. If a relation of fiber burden-causality of mesothelioma is accepted, mesothelioma would be likely caused by amphibole contamination of the plant in 2/12 cases and by the mineral fibers (tremolite and chrysotile) from the mine site in the 10 other cases.

Code(s): 2.
Levin, J. L., M. F. O'Sullivan, C. J. Corn and R. F. Dodson. (1995). "An Individual with a Majority of Ferruginous Bodies Formed on Chrysotile Cores." Archives of Environmental Health, Vol. 50, No. 6, pages 462-465, 19 references, 1995.
Lung samples collected at autopsy from a 59 year old male smoker with bilateral interstitial pulmonary fibrosis and undifferentiated small cell carcinoma at the right lung hilum were found to contain ferruginous bodies, 72% of which had a chrysotile (12001295) core. The remaining bodies were either totally coated or formed on an amphibole fiber. He had been exposed to chrysotile asbestos while working as a clutch rebuilder from 1966 to 1990. He had been employed as an oil derrick worker from 1956 to 1957, and had rebuilt starters and alternators in 1966. He had smoked for 35 to 40 years. He died of respiratory failure after a lung biopsy. The uncoated fiber burden in lung tissue samples was 2,080,000 fibers per grams dry weight. Chrysotile fiber lengths exceeded 8 microns in many cases, and some were as long as 44 microns.

Code(s): 2.
Rodelsperger, K. and H. J. Woitowitz. (1995). "Airborne fibre concentrations and lung burden compared to the tumour response in rats and humans exposed to asbestos." Ann Occup Hyg. 39 (5): 715-25.
The excess risk of tumours exposed to asbestos were previously compared with the results of rat inhalation experiments. It could be demonstrated that humans at the workplace suffer from a tumour risk at fibre concentrations which are 300 times lower than those needed in the rat inhalation model to produce the same risk. However, the estimation of human risk was based on the study of workers

at a chrysotile textile factory, whereas animal experimental results were related to exposure to amphiboles. Since for this comparison the risk of cancer due to exposure to amosite or crocidolite fibres at the workplace is of interest, quantitative exposure-response relationships for lung cancer and mesothelioma for the white workforce of South African amosite and crocidolite mines were discussed. On comparing the risk of lung cancer in this study with the risk of lung cancer for chrysotile textile workers, it can be concluded, that the risk of lung cancer and mesothelioma from crocidolite and amosite was higher than in the chrysotile textile factory. It could be also demonstrated, on the basis of a study of the lung burden of mesothelioma cases and of controls, that a significantly increased odds ratio of about 5 was established at amphibole concentrations of between 0.1 and 0.2 f micrograms-1 dry lung (WHO fibres longer than 5 microns from TEM analysis). On the other hand, carcinogenic response was observed at a fibre concentration 6000 times higher in animal inhalation experiments with crocidolite asbestos (SEM analysis of WHO fibres). As a result of these findings, it has been concluded that inhalation studies in rats are not sufficiently sensitive for the detection of hazards and risks to humans exposed to man-made fibres.

Code(s): 2, 5.
Boillat, M. A. (1999). "[Synthetic mineral fibers]." Schweiz Med Wochenschr. 129 (12): 468-74.
The group of man-made mineral fibres includes slagwool, glasswool, rockwool, glass filaments and microfibres, as well as refractory ceramic fibres. The toxicity of mineral fibres is determined by several factors such as the diameter (< or = 3-3.5 microns) and the length of the fibres (< 100 microns), their biopersistence, which is much shorter for man-made mineral fibres than for asbestos fibres, their physicochemical structure and surface properties, and the exposure level. The chemical composition of the various types of man-made mineral fibres depends directly on the raw material used to manufacture them. While naturally occurring fibres are crystalline in structure, most man-made mineral fibres are amorphous silicates combined with various metal oxides and additives. Observations using intracavitary administration have provided evidence that some types of man-made mineral fibres are bioactive in cellular and animal experiments and may induce lung tumours and mesothelioma. It is difficult to extrapolate these results to humans since they bypass inhalation, deposition, clearance and translocation mechanisms. Inhalation studies show more realistic results but differences are observed between animal species regarding their sensibility to tumours. There is no firm evidence that exposure to various wools is associated with lung fibrosis, pleural lesions or nonspecific respiratory disease in humans. A possible exception may be mentioned for refractory ceramic fibres. A slightly elevated standard mortality ratio for lung cancer has been documented in large cohorts of workers (USA, Europe and Canada) exposed to man- made mineral fibres, especially in the early technological phase. It is not possible to determine from these data whether the risk of lung cancer is due to the man-made mineral fibres themselves, in particular due to the lack of data on smoking habits. No increased risk of mesothelioma has been demonstrated in these cohorts. Epidemiological data are insufficient at this time concerning neoplastic diseases in refractory ceramic fibres.

Code(s): 3.
Wright, R. S., J. L. Abraham, P. Harber, B. R. Burnett, P. Morris and P. West. (2002). "Fatal asbestosis 50 years after brief high intensity exposure in a vermiculite expansion plant." Am J Respir Crit Care Med. 165 (8): 1145-9.
The authors report the case of a 65-year-old accountant whose only asbestos exposure was during a summer job 50 years earlier in a California vermiculite expansion plant. Vermiculite is a silicate material that is useful in building and agriculture as a filler and insulating agent. He developed extensive fibrocalcific pleural plaques and end-stage pulmonary fibrosis, with rapidly progressive respiratory failure. Careful occupational and environmental history revealed no other source of asbestos exposure, and the initial clinical diagnosis was idiopathic pulmonary fibrosis; open lung biopsy shortly before his death confirmed asbestosis. Electron microscopic lung fiber burden analysis revealed over 8,000,000 asbestos fibers per gram dry lung, 68% of which were tremolite asbestos. Additional asbestiform fibers of composition not matching any of the standard asbestos varieties were also present at over 5,000,000 fibers per gram dry lung. Comparison analysis of a sample of Libby, Montana, vermiculite showed a similar mix of asbestiform fibers including tremolite asbestos. This case analysis raises several concerns: risks of vermiculite induced disease among former workers of the more than 200 expansion plants throughout the United States; health effects of brief but very high-intensity exposures to asbestos; and possible health effects in end-users of consumer products containing vermiculite.

Code(s): 3.
Luster, M. I. and P. P. Simeonova. (1998). "Asbestos induces inflammatory cytokines in the lung through redox sensitive transcription factors." Toxicol Lett; 102-103:271-5 1998.
Studies are summarized demonstrating that the inflammatory cytokines, interleukin IL-6 and IL-8, play a direct role in asbestos lung diseases and are produced by lung epithelial cells in direct response to the fibers. This response is controlled by changes in the cellular oxidative/state induced by iron present in the fiber through Fenton-type chemistry. As a result of this oxidative stress, the redox sensitive transcription factors, NF-kappaB and NF-IL-6, which help regulate cytokine gene expression, are activated.

Code(s): 3.
Timblin, C. R., Y. M. Janssen, J. L. Goldberg and B. T. Mossman. (1998). "GRP78, HSP72/73, and cJun stress protein levels in lung

epithelial cells exposed to asbestos, cadmium, or H2O2." Free Radical Biology & Medicine; 24 (4). 1998. 632-642.
BIOSIS COPYRIGHT: BIOL ABS. Occupational exposure to crocidolite asbestos is associated with the development of nonmalignant and malignant pulmonary disease. Considerable evidence indicates that the mechanisms of asbestos-induced toxicity involve the production of active oxygen species (AOS). Production of AOS in excess of cellular defenses creates an environment of oxidative stress and stimulates the expression of a number of different genes whose products may be involved in mediating responses from oxidant injury. To further investigate the mechanisms of asbestos-induced pathogenicity, we have examined by Western blot analyses the induction of the stress response proteins GRP78 and HSP72/73 in rat lung epithelial cells (RLE) exposed to crocidolite asbestos. In comparative studies, we also examined GRP78, HSP72/73, and c-Jun expression in RLE cells exposed to equitoxic concentrations of cadmium chloride (CdCl2) and hydrogen peroxide (H2O2). Our results demonstrate that asbestos and H2O2 do not al

Code(s): 3.
Wang, R., G. Xiao, Z. Ma, H. Qiu and Z. Xiang. (1998). "Effects of Chrysotile Fibres Lipid Peroxides Reaction in Exposed Female Workers and in Rat Lung Macrophages." Chinese Medical Journal (English Edition); 111 (2). 1998. 179.
Biosis copyright: biol abs. rrm note research article rat human female worker patient lung macrophages chrysotile fiber occupational exposure toxin lipid peroxidation asbestosis malondialdehyde lipid peroxidation indicator plasma superoxide dismutase activity antioxidant glutathione peroxidase occupational health respiratory system toxicology asbestos blood and lymphatics immune system toxicity respiratory system disease

Code(s): 3.
Alonso-Peces, M. E., M. A. Juretschke, J. De Miguel, E. Prats, N. Abad and J. A. Serrano. (1997). "Correlation between Radiological and Functional Findings in Workers Exposed to Asbestos Role for High Resolution Computed Tomography Hrct in the Early Diagnosis of Asbestosis." Annual Congress of the European Respiratory Society, Berlin, Germany, September 20-24, 1997. European Respiratory Journal Supplement; 10 (25). 1997. 233s.
Biosis copyright: biol abs. rrm meeting abstract meeting poster human patient pulmonary medicine asbestos high resolution computed tomography asbestosis diagnosis toxicology diagnostic method toxicity respiratory system disease

Code(s): 3.
Brody, A. R., J. B. Mangum and J. I. Everitt. (1997). "Chrysotile asbestos and H2O2 increase permeability of alveolar epithelium. AU - GARDNER SY." Experimental Lung Research; 23 (1). 1997. 1-16.
BIOSIS COPYRIGHT: BIOL ABS. The alveolar epithelium contains tight junctions and provides a barrier to passage of potentially injurious substances into the pulmonary interstitium. Alveolar epithelial injury is hypothesized to be an important early event in the pathogenesis of asbestosis. Mechanisms that may contribute to alveolar epithelial cell injury following asbestos exposure include the physicochemical interactions between asbestos fibers and cells, and the generation of reactive oxygen species such as hydrogen peroxide (H2O2). The present study examined changes in transepithelial resistance (Rt) (a measure of barrier function) and permeability of alveolar epithelium after chrysotile asbestos and H2O2 exposure. Alveolar epithelial cell monolayers, obtained from isolation of rat alveolar type II cells and grown on porous supports, were exposed to chrysotile asbestos or polystyrene beads (control) at concentrations of 5, 10, and 25 mug/cm2 for 24 h. In separate experiments, monolayers were expo

Code(s): 3.
Galani, V., Y. Dalavanga, M. Frangou-Lazaridou, C. Manda-Stachouli, O. Kotoulas and S. H. Constantopoulos. (1997). "Inhabitants of Metsovo Greece Environmentally Exposed to Asbestos Reveal Additional Proteins in Bal Fluid Only When Pleural Calcifications Are Present Another Evidence of Protection against Neoplasia?" Annual Congress of the European Respiratory Society, Berlin, Germany, September 20-24, 1997. European Respiratory Journal Supplement; 10 (25). 1997. 20s.
Biosis copyright: biol abs. rrm meeting abstract human patient pulmonary medicine asbestos environmental exposure toxin bal fluid proteins pleural calcifications neoplasia toxicology respiratory system disease toxicity protection neoplastic disease metsovo greece

Code(s): 3.
Kamp, D. W. and S. A. Weitzman. (1997). "Asbestosis: Clinical spectrum and pathogenic mechanisms." Proceedings of the Society for Experimental Biology and Medicine; 214 (1). 1997. 12-26.
BIOSIS COPYRIGHT: BIOL ABS. Asbestosis is a diffuse pulmonary fibrotic process caused by the inhalation of asbestos fibers. Despite extensive investigations, the precise mechanisms regulating asbestos-induced lung damage are not fully understood. This review summarizes the important clinical manifestations and pathogenic mechanisms of asbestosis. We focus on the relatively new information that has emerged over the last several years. The diagnosis of asbestosis is often easily established by well-characterized criteria. Pulmonary physiologic testing and high-resolution computed tomography can detect clinically occult disease. The finding of asbestos bodies in the bronchoalveolar lavage fluid confirms that an individual has been exposed to asbestos but is of unclear significance in diagnosing asbestosis. Evidence reviewed herein suggests that asbestos pulmonary toxicity is due in part to the physical

properties of the fibers, iron-catalyzed reactive oxygen species (ROS), and macrophage-derived cyto

Code(s): 3.
Karakoca, Y., S. Emri, A. K. Cangir, M. Er, S. Findik and Y. I. Baris. (1997). "Environmental Pleural Plaques Due to Asbestos and Fibrous Zeolite Exposure in Turkey." Annual Congress of the European Respiratory Society, Berlin, Germany, September 20-24, 1997. European Respiratory Journal Supplement; 10 (25). 1997. 20s.
Biosis copyright: biol abs. rrm meeting abstract human patient pulmonary medicine environmental pleural plaques asbestos toxin fibrous zeolite toxicology toxicity respiratory system disease turkey palearctic region

Code(s): 3.
Rocskay, A. Z., M. R. Harbut, M. A. Green, D. L. Osher and E. T. Zellers. (1996). "Respiratory health in asbestos-exposed ironworkers." American Journal of Industrial Medicine; 29 (5). 1996. 459-466.
BIOSIS COPYRIGHT: BIOL ABS. This study aimed to determine the prevalence of respiratory morbidity among asbestos-exposed ironworkers and to determine the relationship between respiratory morbidity indices and length of exposure. A medical screening provided information on chest radiographic abnormalities, pulmonary function, rales, finger clubbing, and respiratory symptoms for 547 asbestos-exposed ironworkers. Union pension records furnished data on length of exposure. The study group exhibited an increased prevalence of small irregular opacities, pleural plaques, and pleural thickening on chest x-ray; reduced FEF25-75; rales; and respiratory symptoms. After controlling for the effect of cigarette smoking and age, years since joining the ironworkers union were significantly associated with profusion, pleural thickening, pleural plaques, rales, percent predicted FVC, reduced FVC, reduced FEV1, reduced FEV1, and dyspnea grades I, II, III, and IV.

Code(s): 3.
Van Cleemput, J., J. Verschakelen, J. Rombouts, R. Masschelein, B. Nemery and L. M. Lacquet. (1996). "Surface of Pleural Plaques Quantitated by Ct-Scanning Relation with Cumulative Asbestos Exposure and Effects on Lung Function." Annual Congress European Respiratory Society, Stockholm, Sweden, September 7-11, 1996. European Respiratory Journal Supplement; 9 (23). 1996. 248s-249s.
Biosis copyright: biol abs. rrm meeting abstract human adult asbestos cement factor worker middle age occupational health computed tomography scanning asbestos cumulative exposure occupational exposure pleural plaques lung function index toxicology asbestosis diagnostic method toxicity respiratory system disease

Code(s): 3.
Zejda, J. E. (1996). "Occupational Exposure to Dusts Containing Asbestos and Chronic Airways Disease." International Journal of Occupational Medicine and Environmental Health, Vol. 9, No. 2, pages 117-125, 50 references, 1996.
The relationship between occupational exposure to asbestos (1332214) containing dusts and chronic airway diseases was discussed. The discussion was based on a review of published studies examining relationships between asbestos dust exposure and deficits in one second expiratory volume (FEV1), used as the 'gold standard' of ventilatory capacity in epidemiological studies examining the effects of occupational exposure on pulmonary function. It was noted that, although few epidemiological studies have specifically addressed the question of whether functional deficits in the peripheral airways can be related to occupational asbestos exposure, this view has gradually obtained support in recent years. The evidence for this view comes from clinical studies reporting an association between impairment in single breath nitrogen index with increasing asbestos exposure, the frequent finding of a disrupted maximum midexpiratory flow in nonsmoking shipyard workers, significant decreases in upstream airflow conductance at low lung volumes in nonsmoking chrysotile (12001295) workers, and a significant association of exposure with reduced flows at long lung volumes. Most of the extant epidemiological studies have shown that FEV1 and forced vital capacity (FVC) in asbestos workers decrease in an exposure dependent manner. Cross sectional studies in particular have shown that decrements in midexpiratory flows can be related to exposure to asbestos containing dusts, an outcome not explained by smoking or the presence of interstitial lung fibrosis. The results of cross sectional studies of lung function conducted in large groups of asbestos cement workers were discussed. These have a shown a clear association between deficits in FEV1 and FVC that are not explained by smoking. The FEV1 and FVC decrements have been found in workers with normal chest X-rays. The author concludes that occupational exposure to asbestos containing dusts can result in chronic disruption of airway function that can be associated with the development of chronic airway disease.

Code(s): 3.
Pierre, N., Y. Iwatsubo, J. Ameille, S. Cordier, L. Mandereau, A. Raix, M. Freddy, A. Delage, J. Bignon and P. Brochard. (1995). "Radiological abnormalities in a cohort of subjects working in asbestos-insulated buildings." Revue D'epidemiologie Et De Sante Publique; 43 (5). 1995. 432-443.
BIOSIS COPYRIGHT: BIOL ABS. The respiratory effects of environmental pollution by asbestos was examined in a cohort of subjects working inside university buildings partly insulated with asbestos containing materials (University of Jussieu in Paris). The present study concerned 727 subjects having undergone two standard radiographic examinations (postero-anterior and oblique chest

x-ray) in the period 1981-1992. The first examination was realized between 01/01/81 and 31/12/85 and the second examination took place between 01/01/86 and 31/12/92. The subjects were classified into three groups according to their exposure status: the group G1 consisted of 161 workers occupationally exposed to asbestos; the group G2 comprised 416 subjects working for at least 15 yr in asbestos-insulated buildings without known occupational exposure to asbestos; the group G3 consisted of 150 workers working for at least 15 yr in the university with no known exposure to asbestos. Whatever the radiological abnormalities con

Asbestos-related, cancer (4, 5, 6)
—health/irritant effects, metabolism, mechanisms

Code(s): 4, 5.
Schneider, J., K. Rodelsperger, B. Bruckel, J. Kleineberg and H. J. Woitowitz. (2001). "Pleural mesothelioma associated with indoor pollution of asbestos." J Cancer Res Clin Oncol. 127 (2): 123-7.
This case report concerns a 46-year-old woman, dying from histologically confirmed diffuse malignant mesothelioma after asbestos exposure, which was only caused by indoor pollution from crocidolite- containing spray asbestos in building materials. There was no other known occupational or environmental asbestos exposure during her life. The lung tissue fibre analysis by light microscopy showed significantly increased concentrations of ferruginous bodies (3162 FB per gram of wet lung tissue). By use of scanning transmission electron microscopy, clearly increased concentrations of amphibole fibres (8.6 x 10(6) fibres longer than 1 microm and 0.6 x 10(6) fibres longer than > or =5 microm per gram dry tissue), mainly classified as crocidolite, were observed. The disease was attributed to indoor exposure to sprayed asbestos, which occurred during her work as a decorator in the studio of a warehouse.

Code(s): 4, 5.
Murai, Y., M. Kitagawa, K. Matsui, F. Koizumi and A. Miwa. (1995). "Asbestos fiber analysis in nine lung cancer cases with high asbestos exposure." Arch Environ Health. 50 (4): 320-5.
We examined the types and sizes of 100 asbestos fibers in lung tissue obtained from 9 lung-cancer cases (5 autopsy and 4 surgical) with more than 10(4) asbestos bodies per 5 g of wet lung tissue, asbestos bodies in histological sections, and the history of occupational asbestos exposure. Evaluation of asbestos fibers by transmission electron microscopy (2,000 x magnification) revealed that most fibers were longer than 3 microns (96%) and were thicker than 0.1 micron (93%). The analytical conditions we used enabled us to identify 99.7% of all asbestos fibers as being amphibole asbestos. Crocidolite fiber, which was found most frequently (73.1%), was the predominant type of fiber found in 8 of the 9 cases; crocidolite was followed by amosite (21.7%), which was the predominant type found in the remaining case. Crocidolite fibers were thin and had a high aspect ratio (mean diameter = 0.23 micron, mean aspect ratio [length/diameter] = 85.5). Amosite fibers were long, and they also had a high aspect ratio (mean length = 21.8 microns, mean aspect ratio = 66.4). It has been suggested that such fibers with a high aspect ratio are strongly carcinogenic to pulmonary parenchyma. Review of our previous and present data with respect to the ratio of amosite to crocidolite fibers in groups of subjects who had various diseases revealed that this ratio was relatively constant in some occupations. The more predominant fibers found were crocidolite in insulation workers and amosite in railroad workers. The ratio of amosite to crocidolite fibers should be considered in tissue-burden studies.

Code(s): 5.
Rodelsperger, K., A. Mandi, A. Tossavainen, B. Bruckel, P. Barbisan and H. J. Woitowitz. (2001). "Inorganic fibres in the lung tissue of Hungarian and German lung cancer patients." Int Arch Occup Environ Health. 74 (2): 133-8.
OBJECTIVE: To ascertain the lung burden of asbestos fibres in Hungarian lung cancer patients in comparison with the cumulative asbestos exposure estimated from the occupational history. METHODS: For 25 Hungarian lung cancer patients, lung tissue fibre analysis was performed by scanning transmission electron microscopy (STEM) and counting of ferruginous bodies (FBs) by light microscopy. Cumulative asbestos exposure in fibre-years was assessed from a standardised occupational history using the report "fibre years" of the German Berufsgenossenschaften. RESULTS: Median and maximum concentrations of fibres longer 5 microns per gram dry lung tissue (g dry) were 0.03 and 7.38 million fibres/g dry for chrysotile, 0.00 and 0.21 million fibres/g dry for amphibole and 0.22 and 0.62 million fibres/g dry for other mineral fibres (OMFs). The maximum values were observed in one patient for whom a high asbestos exposure was evident in advance from the occupational history. CONCLUSIONS: In comparison with reference values obtained by the same method for German patients with no indication of workplace asbestos exposure, increased concentrations of more than 0.2 million chrysotile fibres/g dry were obtained for six of the 25 Hungarian patients (24%). For one of them, the second highest estimate of a workplace exposure of 60 fibre-years and the highest tissue concentration of 7.38 million chrysotile fibres/g dry substantiate a high probability of a causal relationship to asbestos. A further comparison can be made with the results for 66 German patients treated by surgical lung resection for a disorder other than mesothelioma, mainly lung cancer. For the Hungarian lung cancer patients, similar amounts of chrysotile but distinctly lower amounts of amphibole fibres and distinctly higher amounts of OMFs were observed. A correlation between exposure estimates from occupational history and concentration of fibres in the lung tissue was observed for amphibole (Spearman: $R = 0.66$, $P < 0.001$, Pearson: $R = 0.50$, $P = 0.01$) and for chrysotile (Pearson: $R = 0.48$, $P = 0.02$).

Code(s): 5.
Roggli, V. L. (1995). "Malignant mesothelioma and duration of asbestos exposure: correlation with tissue mineral fibre content." Ann Occup Hyg. 39 (3): 363-74.
Among 441 cases of malignant mesothelioma in the author's files, there were 324 for whom reliable information was available regarding the duration of exposure to asbestos. Included were 298 pleural and 26 peritoneal mesotheliomas. The mean duration of exposure to asbestos was 23 +/- 14 years for all cases, and was not different for the pleural and peritoneal groups. Lung tissue was available for analysis of mineral fibre content in 94 cases. Linear regression analysis showed a significant correlation between duration of exposure and asbestos bodies per gramme of wet lung as determined by light microscopy, and between duration of exposure and total uncoated fibres (5 microns or greater in length) as well as commercial amphibole fibres per gramme as determined by scanning electron microscopy ($P < 0.05$). Individuals with direct exposures had on average higher asbestos contents than patients with indirect exposures. Furthermore, for each duration of exposure, shipyard workers had on average higher asbestos contents than non- shipyard workers ($P < 0.05$). Mesotheliomas are associated with a wide range of durations of exposure to asbestos and pulmonary asbestos burdens, and there is a rough correlation between duration of exposure and pulmonary commercial amphibole content.

Code(s): 5, 9.
Yamada, H., H. Hashimoto, M. Akiyama, Y. Kawabata and K. Iwai. (1997). "Talc and amosite/crocidolite preferentially deposited in the lungs of nonoccupational female lung cancer cases in urban areas of Japan." Environ Health Perspect. 105 (5): 504-8.
To analyze the correlation between asbestos lung burden and lung cancer, lungs of 211 female cases with and without lung cancer were examined. Phase-contrast microscopic (PCM) counting of ferruginous (FBs) and uncoated fibers (UFs), which had length longer than 5 microns and aspect ratios greater than 3:1, revealed a significantly higher level of FBs plus UFs in urban lung cancer cases than urban non-lung cancer cases (1380.5 vs. 550.3; $p < 0.001$). No difference was noted between rural lung cancer and non-lung cancer cases. Analytical electron microscopic studies identified various kinds of mineral fibers with an aspect ratio greater than 3:1 in the lung tissue including chrysotile, actinolite/tremolite, amosite/crocidolite, fibrous talc, mica, silica, iron, wollastonite, chlorite, kaoline, and others. The most frequently detected fibers were thin, short chrysotile fibers, most of which could not be found by PCM, followed by relatively thick, long actinolite/tremolite fibers, fibrous talc, and in a smaller number, amosite/crocidolite of intermediate length and width. Amosite/crocidolite and fibrous talc counts in urban lung cancer cases were greater than those of urban non-lung cancer cases, rural lung cancer, and rural non-lung cancer cases; these findings were consistent with PCM analysis. Therefore, it is suggested that fibers detected in PCM observation may be mainly amosite/crocidolite with some parts fibrous talc and that fibrous talc in urban environments may be another candidate for carcinogenic or cocarcinogenic factors of female lung cancer.

Code(s): 5, 11.
Wozniak, H., E. Wiecek, G. Bielichowska-Cybula and B. Opalska. (2001). "[Dust exposure and cancer risk associated with amphibolite mining and processing]." Med Pr. 52 (6): 437-43.
Mining and processing of amphibolite is associated with workers' exposure to dust containing asbestos minerals (actinolite, tremolite) and with the presence of respirable fibers, i.e. small particles above 5 microns long and below 3 microns in diameter (with length-to-diameter ratio higher than 3:1). Results of epidemiological and laboratory studies show that such dust may be responsible for the development of cancer in dust-exposed people. This work reports the measurement results of concentrations of total dust, respirable fibers and mineral composition of samples collected in plant mining and processing amphibolite rock. Based on the results, cumulated exposure was calculated for the 10-, 20- and 30-year exposure periods. The cumulated exposure was classified into two categories: 0.1-1.0 f/cm3 years and 1.0-10 f/cm3. x years. It has been found that mining and processing of amphibolite is associated with increased risk of death from mesothelioma--11.2 x 10(-5) (crushers--10 years of exposure) to 240.0 x 10(-5) (miners--30 years of exposure). The risk of excessive mortality from lung cancer was not high (below 1. x 10(-4)) for all workplaces and periods of exposure.

Code(s): 6.
Marchand, J. L., D. Luce, A. Leclerc, P. Goldberg, E. Orlowski, I. Bugel and J. Brugere. (2000). "Laryngeal and hypopharyngeal cancer and occupational exposure to asbestos and man-made vitreous fibers: results of a case-control study." Am J Ind Med. 37 (6): 581-9.
BACKGROUND: The data from a case-control study performed in France between 1989 and 1991 were used to test whether exposure to either asbestos or to man-made vitreous fibers (MMVF) is a risk factor for cancer of the larynx or the hypopharynx. METHODS: This study involved 315 incident cases of laryngeal cancer, 206 cases of hypopharyngeal cancer, and 305 hospital-based controls with other types of cancer, all recruited in 15 hospitals in six French cities. The subjects' past occupational exposure to asbestos and to four types of MMVF (mineral wool, refractory ceramic fibers, glass filaments, and microfibers) was evaluated based on their job history, with the aid of a job-exposure matrix. Odds ratios were calculated with unconditional logistic regression, with adjustment for smoking and drinking levels. RESULTS: Exposure to asbestos resulted in a significant increase in the risk of hypopharyngeal cancer (OR = 1.80, 95% CI: 1.08-2.99) and a nonsignificant increase in the risk of laryngeal cancer (OR = 1.24, 95% CI: 0.83-1.90). Risk was

highest for the epilarynx (highest cumulative level of exposure: OR = 2.22, 95% CI: 1.05-4.71). Exposure to mineral wools was of borderline significance for the risk of hypopharyngeal cancer (OR = 1.55, 95% CI: 0.99-2.41), and nonsignificantly associated with the risk of laryngeal cancer (OR-1.33, 95% CI: 0.91-1.95). The risk was again highest for the epilarynx (OR = 1.85, 95% CI: 1.08- 3.17). No significant results were observed for the other MMVF. CONCLUSIONS: These results suggest that asbestos exposure increases the risk of epilaryngeal and hypopharyngeal cancers. It is difficult to reach a conclusion about the effects of mineral wools, because nearly all the exposed subjects were also exposed to asbestos. The possible effects of other MMVF were difficult to assess in this study, because of the paucity of exposed subjects.

Code(s): 6.
Goldberg, M. (1999). "[Asbestos and risk of cancer: exposure-effect relationships for occupationally exposed populations]." Rev Mal Respir. 16 (6 Pt 2): 1278-85.
For high levels of exposure (> 1 f/ml), the risk of lung cancer increases linearly with the cumulative exposure, and is the same for all types of asbestos; the risk of mesothelioma increases linearly with the level of exposure, is time dependent and higher for amphiboles. The effects of asbestos and smoking for lung cancer are independent, and the probability that a cancer is due to asbestos is the same among smokers and non-smokers. There is no scientific method for quantifying directly the risks associated to low levels of exposure (< 1 f/ml). The only possible approach is to extrapolate from the risks observed at high levels to low levels. Proportionality without threshold between dose and risk is not certain, but is the most plausible model. Using this model, one can expect about 30 additional cases of cancer for 10,000 men exposed at the level of 0.1 f/ml from 20 to 65 years, and about 16 additional cases for 10,000 women. These are high figures compared to other health hazards.

Code(s): 6.
Goodman, M., R. W. Morgan, R. Ray, C. D. Malloy and K. Zhao. (1999). "Cancer in asbestos-exposed occupational cohorts: A meta-analysis." Cancer Causes & Control; 10 (5). 1999. 453-465.
BIOSIS COPYRIGHT: BIOL ABS. Objective: To examine existing asbestos-exposed occupational cohorts and apply a meta-analytic technique to determine the magnitude of association between exposure and lung cancer and to investigate other cancer sites that may be related to such an exposure. Methods: We summarized the data from 69 asbestos-exposed occupational cohorts reporting on cancer morbidity and mortality. Data were extracted regarding numbers of deaths for each cancer, numbers of mesotheliomas, occupations and latency for osure. Results: Lung cancer data demonstrated meta-SMRs of 163 and 148 with and without latency,respectively, with significant heterogeneity of results even after stratification according to occupational groups. Stratification of lung cancer studies according to percentage of mesothelioma deaths showed a dose-response effect. Z-scores ranged from -12.21 to +29.49. Analysis for laryngeal cancer yielded meta-SMRs of 157 and 133 with and without latency, respectively, demonstrating homogeneous resu lity of the association between occupational asbestos and lung cancer. There was a suggestion of an association between asbestos and laryngeal carcinoma and no clear association with other cancers.

Code(s): 6.
Mzileni, O., F. Sitas, K. Steyn, H. Carrara and P. Bekker. (1999). "Lung cancer, tobacco, and environmental factors in the African population of the Northern Province, South Africa." Tob Control. 8 (4): 398-401.
DESIGN: Case-control study among incident African patients with cancer. Questionnaire assessment of exposure to tobacco, occupation, and place of birth. SETTING: Northern Province, South Africa. SUBJECTS: Between 1993 and 1995, 288 men and 60 women with lung cancer and 183 male and 197 female controls (consisting of patients newly diagnosed with cancers other than those known to be associated with smoking) were interviewed. Unmatched, unconditional logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (95% CIs) of developing lung cancer in relation to a number of variables. MAIN OUTCOME MEASURE: Risk of developing lung cancer related to exposure to tobacco, indoor pollution, dusty work environment, and residential exposure to asbestos. RESULTS: There was a significant increase in the risk of developing lung cancer through smoking. In men, the ORs were 2.2 (95% CI = 1.0 to 4. 6) in ex-smokers, 9.8 (95% CI = 5.9 to 16.4) in light smokers (0-14 g/day), and 12.0 (95% CI = 6.5 to 22.3) in heavy smokers. In women, the ORs were 5.8 (95% CI = 1.3 to 25.8) in ex- smokers and 5.5 (95% CI = 2.6 to 11.3) in current smokers. Work in a dusty industry showed an elevated risk (OR = 3.2, 95% CI = 1.8 to 5.8) for lung cancer only in men. Male residents of areas where asbestos was shipped for distribution (termed moderately polluted asbestos areas) had a 2.5-fold increase (95% CI = 1.0 to 4.4) in the risk (OR) of developing lung cancer, and residents of areas where asbestos was mined (termed heavily polluted asbestos areas) had a 2.8-fold increase in risk (95% CI = 0.7 to 10.4). Female residents of heavily polluted asbestos areas showed elevated risks of 5.4 (95% CI = 1.3 to 22.5) of developing lung cancer. CONCLUSION: The data suggest that tobacco smoking is the most important risk factor for the development of lung cancer in this setting. Risks for lung cancer are reminiscent of those observed in Western countries in the 1960s and 1970s. However, environmental exposure to asbestos, a dusty occupation (in men), and perhaps indoor air pollution may also contribute to the development of lung cancer in this province.

Code(s): 6.

Ollikainen, T., K. Linnainmaa and V. L. Kinnula. (1999). "DNA single strand breaks induced by asbestos fibers in human pleural mesothelial cells in vitro." Environ Mol Mutagen 1999;33(2):153-60.
The mechanisms of the cellular effects and DNA damage caused by asbestos fibers in human mesothelial cells are not well understood. We exposed transformed human pleural mesothelial cells to 1-4 microg/cm2 crocidolite and to 10-100 ng/ml tumor necrosis factor alpha for up to 48 hr and studied the induction of DNA damage using the Comet assay. As a positive control, 100 microM H2O2 was used. The DNA single strand breaks were assessed as the mean tail moments and as distributions of the tail DNA in the cell. The Comet assay showed significant but reversible increases in the mean tail moments, but not in the distribution of Comet tails in the histograms in cells exposed to 1 microg/cm2 crocidolite for 6 hr. At higher concentrations of asbestos fibers all the indices in the Comet assay showed significant and irreversible change. All the doses of TNF-alpha caused marginal increase in the mean tail moments. The mean tail moments were highest in the cells with concurrent treatment to TNF-alpha and crocidolite. In the cells pretreated with inhibitors of antioxidant enzymes (aminotriazole for catalase and buthionine sulfoximine for gamma-glutamylcysteine synthetase) asbestos fibers slightly increased oxidant-related fluorescence of dichlorofluorescein (DCFH) but did not cause any further increases in the mean tail moments. This study shows that asbestos fibers cause DNA single strand breaks in human mesothelial cells. Since the inhibition of antioxidant enzymes did not have an effect on the DNA damage caused by the fibers, other mechanisms than free radicals seem to be involved in the induction of DNA damage by mineral fibers.

Code(s): 6.
Begin, R. (1998). "Asbestos exposure and pleuropulmonary cancer." Revue Des Maladies Respiratoires; 15 (6). 1998. 723-730.
BIOSIS COPYRIGHT: BIOL ABS. Pleuropulmonary cancers are recognized asbestos-related diseases. Mesothelioma occurs almost uniquely in individuals exposed to asbestos whereas lung cancer is strongly associated with smoking. If the asbestos exposure is sufficient however, the incidence of lung cancer is higher than would be expected from the smoking effect alone. For lung cancer in asbestos workers, asbestosis is not a prerequisite for recognition as an occupation-related disease. The intensity and duration of exposure to asbestos are factors associated with higher risk of lung cancer. These factors can be estimated on the basis of the work history or, when necessary, by analyzing mineral dust from available lung tissues.

Code(s): 6.
Kamp, D. W., M. J. Greenberger, J. S. Sbalchierro, S. E. Preusen and S. A. Weitzman. (1998). "Cigarette smoke augments asbestos-induced alveolar epithelial cell injury: role of free radicals." Free Radic Biol Med 1998 Oct;25(6):728-39.
Cigarette smoke augments asbestos-induced bronchogenic carcinoma by mechanisms that are not established. Alveolar epithelial cell (AEC) injury due to oxidant-induced DNA damage and depletion of glutathione (GSH) and adenosine triphosphate (ATP) may be one important mechanism. We previously showed that amosite asbestos-induces hydroxyl radical production and DNA damage to cultured AEC and that phytic acid, an iron chelator, is protective. We hypothesized that whole cigarette smoke extracts (CSE) augment amosite asbestos-induced AEC injury by generating iron-induced free radicals that damage DNA and reduce cellular GSH and ATP levels. Asbestos or CSE each caused dose-dependent toxicity to AEC (WI-26 and rat alveolar type I-like cells) as assessed by 51chromium release. The combination of asbestos (5 microg/cm2) and CSE (0.01-0.1%) caused synergistic injury whereas higher doses of each agent primarily had an additive toxic effect. Asbestos (5 microg/cm2) augmented CSE-induced (0.01-1.0%) AEC DNA damage over a 4 h exposure period as assessed by an alkaline unwinding, ethidium bromide fluorometric technique. These effects were synergistic in A549 cells and additive in WI-26 cells. Asbestos (5 microg/cm2) and CSE (0.5-1.0%) reduced A549 and WI-26 cell GSH levels as assessed spectrophotometrically and ATP levels as assessed by luciferin/luciferase chemiluminescence but a synergistic interaction was not detected. Phytic acid (500 microM) and catalase (100 microg/ml) each attenuated A549 cell DNA damage and depletion of ATP caused by asbestos and CSE. However, neither agent attenuated WI-26 cell DNA damage nor the reductions in GSH levels in WI-26 and A549 cells exposed to asbestos and CSE. We conclude that CSE enhance asbestos-induced DNA damage in cultured alveolar epithelial cells. These data provide additional support that asbestos and cigarette smoke are genotoxic to relevant target cells in the lung and that iron-induced free radicals may in part cause these effects.

Code(s): 6.
Karasaki, Y., H. Urano, A. Shirahata, Z. Nambu, T. Ohji, M. Miura and S. Gotoh. (1998). "Increases in DNA and protein syntheses in human umbilical vein endothelial cells treated with asbestos." Journal of Occupational Health; 40 (4). 1998. 302-306.
BIOSIS COPYRIGHT: BIOL ABS. When human umbilical vein endothelial cells (HUVECs) were treated with crocidolite asbestos, HUVECs phagocytized the fibers; no cytotoxic effect was observed when treated at concentrations lower than 10 mug/ml for 24 h, 48 h and 72 h. The time-dependent effect of crocidolite asbestos on DNA synthesis and protein synthesis in HUVECs was studied. The DNA synthesis of the cells exhibited the maximum augmentation (150%) at 24 h, and the protein synthesis increased to the maximal value (140%) at 36 h. The dose-dependent effect of crocidolite asbestos on DNA synthesis and protein synthesis in HUVECs was also studied. The maximum increases in DNA synthesis and protein synthesis were observed at 5 mug/ml and at 10 mug/ml of the fibers, respectively. An apparent increase in DNA synthesis may be mainly due to the repair of DNA damage induced by asbestos under our present experimental conditions, but also in part due to the mitogenic effect of asbestos. Cell injury and DNA damage

Code(s): 6.
Kitamura, F., S. Araki, T. Tanigawa, H. Miura, H. Akabane and R. Iwasaki. (1998). "Assessment of mutations of Ha- and Ki-ras oncogenes and the p53 suppressor gene in seven malignant mesothelioma patients exposed to asbestos. PCR-SSCP and sequencing analyses of paraffin-embedded primary tumors." Industrial Health; 36 (1). 1998. 52-56.
BIOSIS COPYRIGHT: BIOL ABS. To examine whether malignant mesothelioma due to asbestos has genetic alterations in the Ha- and Ki-ras oncogenes or in the p53 suppressor gene, we analyzed the point mutations of these genes in paraffin-embedded autopsy samples of the primary tumors of malignant mesothelioma in seven asbestos patients who died from malignant mesothelioma. The genetic analysis was conducted by the polymerase chain reaction-single strand conformation polymorphisms (PCR-SSCP) method in all patients, and through the sequencing of deoxyribonucleic acid (DNA) bases in one patient. No genetic alterations were found in exons 1 or 2 of Ha- and Ki-ras oncogenes, or in exons 5 to 9 of the p53 gene, in any of the patients. Further studies on a larger number of patients are required to reach a definite conclusion concerning the genetic effects of asbestos on malignant mesothelioma.

Code(s): 6.
Wang, Q., J. Fan and X. Zhao. (1998). "[Damage effects of asbestos and cigarette smoke solution on human embryo lung cell DNA]." Chung Hua Yu Fang I Hsueh Tsa Chih 1998 Jan;32(1):31-3.
OBJECTIVE: To study the combined damage effects of asbestos and cigarette solution on human embryo lung cell (HEL) DNA. METHODS: Unscheduled DNA synthesis (UDS) assay was used. Repair and synthesis on DNA in HEL treated with asbestos and/or cigarette smoke was studied. RESULTS: It showed that UDS in HEL could be induced by exposure to asbestos or cigarette smoke only with a significant dose-response relationship, and the amounts of [3H]-TdR incorporation in cells treated with combination of asbestos and cigarette smoke was significantly higher than their sum in cells treated with asbestos or cigarette only. CONCLUSION: There is a synergistic damage effect of asbestos and cigarette on DNA of HEL. In addition, dimethyl sulfoxide (DMSO), a scavenger of .OH, can partly inhibit [3H]-TdR incorporation caused by asbestos. And .OH plays certain role in damage to DNA of cells caused by asbestos.

Code(s): 6.
De Vuyst, P., A. Missouni, A. Van Muylem, P. Rocmans and P. Dumortier. (1997). "Systematic Asbestos Bodies Counting in Lung Specimens Resected for Lung Cancer." Annual Congress of the European Respiratory Society, Berlin, Germany, September 20-24, 1997. European Respiratory Journal Supplement; 10 (25). 1997. 19s.
Biosis copyright: biol abs. rrm meeting abstract human patient pulmonary medicine systematic asbestos bodies lung specimens asbestos related lung cancer asbestos carcinogen occupational exposure oncology toxicology respiratory system neoplastic disease respiratory system disease toxicity

Code(s): 6.
Hei, T. K., L. J. Wu and C. Q. Piao. (1997). "Malignant Transformation of Immortalized Human Bronchial Epithelial Cells by Asbestos Fibers." Environmental Health Perspectives, Vol. 105, Supplement 5, pages 1085-1088, 19 references, 1997.
The influence of chrysotile (12001295) fibers on the malignant transformation of human papillomavirus immortalized human bronchial epithelial (BEP2D) cells was examined. The BEP2D cells were cultured with chrysotile fiber doses of 10 or 20 micrograms per milliliter for 7 days. Several assays were applied to the determination of transformed phenotypes. The origin of induced tumor cells in nude mice was determined by immunohistochemical staining. Mutation in the K-ras gene was detected by polymerase chain reaction amplification and restriction enzyme analysis. The clonogenic survival of BEP2D cells was reduced dose dependently by chrysotile fibers. The plating efficiency of control cells was markedly decreased in the presence of serum and the tumor promoter 12-O-tetradecanoylphorbol-13-acetate (TPA). In contrast, the plating efficiency of fiber treated cells was not significantly influenced by the presence of serum and TPA in the cell medium. The saturation density of the transformed and tumorigenic BEP2D cells was higher than that of the control cells. While fiber treated BEP2D cells were not immediately tumorigenic in nude mice, the cells did exhibit tumorigenicity with a latency period of 8 to 10 weeks following extensive subcultivation, during which anchorage independent growth developed. These tumors, representing two primary tumorigenic cell lines, were of epithelial origin. K-ras gene mutations in codon 13 were not detected in the tumorigenic BEP2D cells induced by chrysotile fibers. The authors conclude that BEP2D cells are a useful model for investigating the mechanisms of fiber carcinogenesis in human bronchial epithelial cells.

Code(s): 6.
Howel, D., L. Arblaster, L. Swinburne, M. Schweiger, E. Renvoize and P. Hatton. (1997). "Routes of Asbestos Exposure and the Development of Mesothelioma in an English Region." Occupational and Environmental Medicine, Vol. 54, No. 6, pages 403-409, 18 references, 1997.
In this case control study, the effect of the route of asbestos (1332214) exposure on the development of mesothelioma was examined in four health districts in Yorkshire, England. The subjects consisted of 185 confirmed cases of mesothelioma who died between 1979 and 1991, and 159 controls matched by sex, age, and year of death. The surviving relatives were interviewed concerning the exposure histories of the deceased subjects. Occupational, paraoccupational, and residential asbestos exposures were rated as likely, possible, or

not likely. Likely occupational exposure to asbestos was observed among 56% of the cases and 14% of the controls. Possible occupational asbestos exposure was noted among 81% of the cases and 50% of the controls. Among the mesothelioma cases, odds ratios (ORs) of 9.1 and 5.6 were calculated for likely and likely plus possible asbestos exposure, respectively. Excluding cases of likely occupational exposure, 18 of 81 cases and five of 124 controls had likely paraoccupational asbestos exposure. The OR for likely paraoccupational asbestos exposure with mesothelioma equaled 5.6. Excluding cases of likely and possible occupational exposure, 13 of 34 cases and three of 58 controls had likely paraoccupational asbestos exposure. The OR for likely paraoccupational asbestos exposure with mesothelioma equaled 61.7. Excluding subjects with likely or possible occupational exposure and likely or possible paraoccupational exposure, an OR of 6.6 was calculated for developing mesothelioma with likely residential asbestos exposure. However, the number of subjects in this category was too small to properly determine this relationship. Of the total exposure histories, 45% involved asbestos exposure by more than one route. While 27% of the controls encountered no asbestos exposure, only 5% of the cases encountered no asbestos exposure. The authors conclude that occupational and paraoccupational asbestos exposure is associated with mesothelioma.

Code(s): 6.
Lash, T. L., E. A. Crouch and L. C. Green. (1997). "A meta-analysis of the relation between cumulative exposure to asbestos and relative risk of lung cancer." Occup Environ Med. 54 (4): 254-63.
OBJECTIVES: To obtain summary measures of the relation between cumulative exposure to asbestos and relative risk of lung cancer from published studies of exposed cohorts, and to explore the sources of heterogeneity in the dose-response coefficient with data available in these publications. METHODS: 15 cohorts in which the dose-response relation between cumulative exposure to asbestos and relative risk of lung cancer has been reported were identified. Linear dose-response models were applied, with intercepts either specific to the cohort or constrained by a random effects model; and with slopes specific to the cohort, constrained to be identical between cohorts (fixed effect), or constrained by a random effects model. Maximum likelihood techniques were used for the fitting procedures and to investigate sources of heterogeneity in the cohort specific dose-response relations. RESULTS: Estimates of the study specific dose-response coefficient (kappa 1.i) ranged from zero to 42 x 10(-3) ml/fibre-year (ml/f-y). Under the fixed effect model, a maximum likelihood estimate of the summary measure of the coefficient (k1) equal to 0.42 x 10(-3) (95% confidence interval (95% CI) 0.22 to 0.69 x 10(-3)) ml/f-y was obtained. Under the random effects model, implemented because there was substantial heterogeneity in the estimates of kappa 1.i and the zero dose intercepts (Ai), a maximum likelihood estimate of k1 equal to 2.6 x 10(-3) (95% CI 0.65 to 7.4 x 10(-3)) ml/f-y, and a maximum likelihood estimate of A equal to 1.36 (95% CI 1.05 to 1.76) were found. Industry category, dose measurements, tobacco habits, and standardisation procedures were identified as sources of heterogeneity. CONCLUSIONS: The appropriate summary measure of the relation between cumulative exposure to asbestos and relative risk of lung cancer depends on the context in which the measure will be applied and the prior beliefs of those applying the measure. In most situations, the summary measure of effect obtained under the random effects model is recommended. Under this model, potency, k1, is fourfold lower than that calculated by the United States Occupational Safety and Health Administration.

Code(s): 6.
Maltoni, C. (1997). "The Long-Lasting Legacy of Industrial Carcinogens: The Lesson of Asbestos. Irving J. Selikoff Memorial Lecture, 1995." Annals of the New York Academy of Sciences, Vol. 837, pages 570-586, 9 references, 1997.
The long term effects of carcinogenic industrial agents, namely asbestos (1332214), were discussed. Cancer was described as the major public health hazard of the present time. Cancer was considered to be primarily an environmental disease, related to the industrial generation of carcinogenic substances. Only in recent years were industrial agents tested for carcinogenicity prior to use. Therefore, exposure to carcinogenic industrial agents in past decades was largely uncontrolled. Because of these past exposures, most countries had a significant legacy of cancer risk. Asbestos, a known carcinogen, was used extensively by various industries during the past century. Despite the well established risks, many countries, especially developing countries, continued to use asbestos. In addition to other tumor types, asbestos exposure caused the otherwise very rare mesothelioma. Epidemiological studies revealed the substantial risk of asbestos related cancers among exposed workers in various occupations. Nonoccupational, family, home, and environmental exposure to asbestos also led to increased cancer risk. The author concludes that the legacy of carcinogenic industrial agents, such as asbestos, may be long lasting, affecting the present generation and many generations to come.

Code(s): 6.
Szesznia-Dabrowska, N., U. Wilczynska and W. Szymczak. (1997). "Cancer risk in the asbestos-cement industry workers in Poland." Medycyna Pracy; 48 (5). 1997. 473-483.
BIOSIS COPYRIGHT: BIOL ABS. A cohort study was carried out in order to evaluate the cancer risk in the asbestos-cement industry workers. The cohort consisted of workers employed in four asbestos-cement plants. One of those plants was established in 1924, the other three in the 1960s and 1970s. Currently only two of these plants continue their production. The plants used mainly chrysotile asbestos as well as crocidolite and amosite. Amphibolite asbestos was used before the mid-nineteen eighties in production of pressure pipes utilising about 15% of the total quantity of asbestos used. The measurements of the asbestos fibre concentration at work-sites

have been taken occasionally since the mid 1980s, thus, the determination of a cumulative dose for individual persons in the cohort and the evaluation of the dose-effect relationship were not feasible. It could only be supposed that the concentrations at the preparatory work-site during first years of the plants' operation accounted for several tens fi

Code(s): 6.
Coplu, L., P. Dumortier, A. U. Demir, Z. T. Selcuk, F. Kalyoncu, G. Kisacik, P. DeVuyst, A. A. Sahin and Y. I. Baris. (1996). "An epidemiological study in an Anatolian village in Turkey environmentally exposed to tremolite asbestos." J Environ Pathol Toxicol Oncol. 15 (2-4): 177-82.
After several cases of malignant pleural mesothelioma (MPM) were detected in the village of Kureysler in the Kutahya district of western Turkey, an epidemiological study was conducted. A questionnaire was completed by 124 villagers who were older than 20 years and standard posteroanterior chest X-rays were taken. The films were evaluated by three chest physicians. Samples of the white stucco that had been used by almost all villagers for indoor painting for many years were mineralogically examined. Chest X-rays showed that 23 (18%) had pleural plaques and calcifications compatible with asbestos exposure. Male sex and old age were associated with occurrence of pleural plaques. An analysis of white stucco samples revealed tremolite asbestos. In conclusion, tremolite fibers might be the cause of the high incidence of pleural plaques and MPM cases in the village of Kureysler.

Code(s): 6.
De Klerk, N. H., A. W. Musk, J. L. Eccles, J. Hansen and M. S. Hobbs. (1996). "Exposure to crocidolite and the incidence of different histological types of lung cancer." Occupational and Environmental Medicine; 53 (3). 1996. 157-159.
BIOSIS COPYRIGHT: BIOL ABS. Objectives-To estimate the relations between exposure to both tobacco smoke and crocidolite and the incidence of various histological types of lung cancer. Methods-In 1979 all former workers from the Wittenoom asbestos industry who could be traced were sent a questionnaire on smoking history. Of 2928 questionnaires sent, satisfactory replies were received from 2400 men and 149 women. Of the men, 80% had smoked at some time and 50% still smoked. Occupational exposure to crocidolite was known from employment records and follow up was maintained through death and cancer registries in Australia with histological diagnoses obtained from the relevant State Cancer Registry. Conditional logistic regression was used to estimate the effects of tobacco and asbestos exposure on incidence of different cell types of lung cancer in a nested case-control design. Results-Between 1979 and 1990, 71 cases of lung cancer occurred among men in this cohort: 27% squamous cell carcinoma, 31% a

Code(s): 6.
D[illegible]onmez, H., Y. Ozkul and R. U[illegible]cak. (1996). "Sister chromatid exchange frequency in inhabitants exposed to asbestos in Turkey." Mutat Res 1996 Dec 12;361(2-3):129-32.
Pleural mesothelioma, lung cancer, pleural calcification and fibrosis have been observed among inhabitants of the villages in Ivriz-Zanapa valley in Turkey. Earlier reports have stated that these endemic pathological conditions are caused by the inhalation of actinolite asbestos, a mineral commonly used indiscriminately to paint the walls and floors of houses. In the present study, 40 inhabitants in Yassikaya village in Ivriz-Zanapa valley and 20 controls were further investigated. The peripheral blood lymphocytes were cultured and harvested at 72 h for sister chromatid exchange (SCE) frequency. Inhabitants had a raised mean SCE rate compared with a control population.

Code(s): 6.
Jones, R. N., J. M. Hughes and H. Weill. (1996). "Asbestos Exposure Asbestosis and Asbestos-Attributable Lung Cancer." Thorax; 51 (Suppl. 2). 1996. S9-S15.
Biosis copyright: biol abs. rrm literature review human patient lung cancer asbestos asbestos exposure asbestosis toxicology pulmonary medicine diagnosis neoplastic disease asbestos-attributable respiratory system disease toxicity

Code(s): 6.
Gilmour, P. S., P. H. Beswick, D. M. Brown and K. Donaldson. (1995). "Detection of surface free radical activity of respirable industrial fibres using supercoiled phiX174 RF1 plasmid DNA." Carcinogenesis (Oxford); 16 (12). 1995. 2973-2979.
BIOSIS COPYRIGHT: BIOL ABS. The ability of a number of respirable industrial fibres, amosite and crocidolite asbestos, refractory ceramic fibres (RCFs) and man-made vitreous fibres (NIMVFs), to cause free radical injury to plasmid phiX174RFI DNA was assessed. The oxidative DNA damage was observed as depletion of supercoiled DNA after fibre treatment and was quantified by scanning laser densitometry. The mechanism of fibre-mediated damage was determined by the use of the specific hydroxyl radical scavenger mannitol and the iron chelator desferrioxamine-B. The amosite and crocidolite asbestos caused substantial damage to DNA that was dose-related. The free radicals responsible for the asbestos-mediated DNA damage were hydroxyl radicals, as determined by inhibition with mannitol. Asbestos fibre-mediated damage to DNA was completely ameliorated by the chelation of fibre-associated iron with desferrioxamine-B. The amount of Fe(II) and Fe(III) released by equal numbers of the different fibre types at eq

Code(s): 6.
Maltoni, C., C. Pinto, R. Carnuccio, D. Valenti, P. Lodi and E. Amaducci. (1995). "Mesotheliomas following exposure to asbestos used in railroads: 130 Italian cases." Med Lav. 86 (5): 461-77.
The available knowledge on the oncogenic risks of asbestos, the data on the uses of asbestos in railroads, with particular regard to the Italian State Railroads (Ferrovie dello Stato = FS), and the groups at risk due to the exposure to asbestos used in railroads were briefly reviewed. The available data on the pathological effects of such exposure, and particularly on the onset of mesotheliomas among machinists and other railroad workers, were also summarized. One hundred and thirty cases of mesothelioma (122 pleural, 1 pericardial, 6 peritoneal and 1 pleuro-peritoneal), related to the exposure to asbestos used in railroads, observed in various Italian regions, were reported. Fifty-three of these cases (among which 49 reported in the Emilia Romagna Region) were submitted to a detailed study at the Bologna Institute of Oncology. Seventy-seven cases of mesothelioma occurred among occupationally exposed FS workers, in particular machinists; 45 cases occurred among rolling-stock machinists and workers engaged in the repair and demolition of the rails of workshops not belonging to the FS; 3 cases occurred among travelling workers of rolling-stock, not belonging to the FS; and 5 cases were found in family members (1 daughter, 3 wives and 1 sister) of railroad workers. This series of cases, together with similar data from the literature, proves the existence of an actual health risk due to asbestos used in railroads, and indicates its gravity. On the basis of the available data, the following steps are considered necessary: the promotion of systematic epidemiological investigations, the adoption of preventive measures, the performance of medical oncological surveillance, and the automatic compensation for tumours following the exposure to the asbestos used in railroads.

Code(s): 6.
Rogers, A. and M. Nevill. (1995). "Occupational and Environmental Mesotheliomas due to Crocidolite Mining Activities in Wittenoom, Western Australia." Scandinavian Journal of Work, Environment and Health, Vol. 21, No. 4, pages 259-264, 19 references, 1995.
The risk associated with residual crocidolite (12001284) fibers in the area around Wittenoom, Australia was calculated in 1992 and updated for observed mesothelioma cases to June 1994. Mesothelioma cases were extracted from the 2,398 case reports of the Australian Mesothelioma Surveillance Program. Current airborne fiber concentrations were estimated. Most of the mesothelioma cases (72%) resulted from direct occupational exposure in mines or mills. Another 11% of cases resulted from handling or transporting raw fiber or using tailings in road construction, which continued into the 1970s. Five percent of mesotheliomas were found in nonmine employees. Environmental mesotheliomas (10%) occurred in women and children and visitors to the town. In the period 1992 to 1994, 32 new cases were notified. The latency period was 30 to 40 years. Incidence rates were calculated as 67.9 per person 1,000 years for employees at the mine site; 5.9 per person 1,000 years for residential adult females; and 3.2 per person 1,000 years for residential children. It was estimated that the risk of developing mesothelioma due to visiting the Wittenoom Gorge and the national park is of the same order of magnitude as other nonasbestos risks in the area. The authors conclude that occupational and environmental induced lung cancer and mesothelioma will continue to be observed as a result of latency effects from past exposures and residual contamination of the township.

Code(s): 6.
Schneider, J., K. Grossgarten and H. J. Woitowitz. (1995). "[Fatal pleural mesothelioma diseases caused by familial household contacts with asbestos fiber dust]." Pneumologie. 49 (2): 55-9.
The case histories of a family are described where 3 out of 4 developed asbestos-related diseases. Only the husband had direct occupational exposure handling blue-asbestos materials while working in a producing insulating factory in 1950-59. He died of pulmonary asbestosis as an occupational disease. His wife and his son died of asbestos related mesothelioma. Detailed exposure history revealed exposure to asbestos by laundering her husband's contaminated working clothes. His son was exposed to asbestos during childhood by helping his mother laundering the father's working clothes and in addition by visiting his father's working place regularly. The significance of nonoccupational exposure to asbestos is emphasized as a causative factor in the development of malignant mesothelioma.

Code(s): 6.
Schneider, J. and H. J. Woitowitz. (1995). "[Asbestos-related mesotheliomas in housewives from indoor air pollution]." Zentralbl Hyg Umweltmed. 196 (6): 495-503.
We report five cases of pleural mesothelioma in housewives, that are attributed to inhalative household-contact with asbestos. An occupational history of asbestos exposure could not be revealed. A causal relationship between the fatal disease and the inhalative house- hold-contact with asbestos was established based on the cleaning of asbestos contaminated work-clothes of the husbands.

Code(s): 6.
Szeszenia-Dabrowska, N., W. Szymczak and U. Wilczynska. (1995). "[Assessment of lung cancer risk due to environmental asbestos dust exposure in the general population]." Przegl Epidemiol. 49 (4): 407-16.

Suggested "Charge" Publications
ERG Has in Possession

2. Hart, G. A., L. M. Kathman and T. W. Hesterberg. (1994). "In vitro cytotoxicity of asbestos and man-made vitreous fibers: roles of fiber length, diameter and composition." Carcinogenesis. 15 (5): 971-7.

4. Maxim, L. D. and E. E. McConnell. (2001). "Interspecies comparisons of the toxicity of asbestos and synthetic vitreous fibers: a weight-of-the-evidence approach." Regul Toxicol Pharmacol. 33 (3): 319-42.

6. Osinubi, O. Y., M. Gochfeld and H. M. Kipen. (2000). "Health effects of asbestos and nonasbestos fibers." Environ Health Perspect. 108 Suppl 4 665-74.

8. Rodelsperger, K., K. H. Jockel, H. Pohlabeln, W. Romer and H. J. Woitowitz. (2001). "Asbestos and man-made vitreous fibers as risk factors for diffuse malignant mesothelioma: results from a German hospital-based case- control study." Am J Ind Med. 39 (3): 262-75.

10. Gilmour, P. S., D. M. Brown, P. H. Beswick, W. MacNee, I. Rahman and K. Donaldson. (1997). "Free radical activity of industrial fibers: role of iron in oxidative stress and activation of transcription factors." Environ Health Perspect. 105 Suppl 5 1313-7.

13. Oberdorster, G. (2000). "Determinants of the pathogenicity of man-made vitreous fibers (MMVF)." Int Arch Occup Environ Health. 73 Suppl S60-8.

14. Lockey, J. E. (1996). "Man-Made Fibers and Nonasbestos Fibrous Silicates." Occupational and Environmental Respiratory Disease, P. Harber, M. B. Schenker and J. R. Balmes, Eds; Mosby-Year Book, Inc., St. Louis, MO, pp 330-344, 101 refs.

16. Hesterberg, T. W. and G. A. Hart. (2001). "Synthetic vitreous fibers: a review of toxicology research and its impact on hazard classification." Crit Rev Toxicol. 31 (1): 1-53. [Haven't printed yet because it's 45 pages long.]

18. Carter, C. M., C. W. Axten, C. D. Byers, G. R. Chase, A. R. Koenig, J. W. Reynolds and K. D. Rosinski. (1999). "Indoor airborne fiber levels of MMVF in residential and commercial buildings." Am Ind Hyg Assoc J. 60 (6): 794-800.

20. Morgan, A. (1995). "Deposition of Inhaled Asbestos and Man-Made Mineral Fibres in the Respiratory Tract." Annals of Occupational Hygiene, Vol. 39, No. 5, pages 747-758, 40 references, 1995.

Assessment of lung cancer risk due to environmental asbestos dust exposure in the general population was based on the model of risk extrapolation from the occupational (in asbestos-cement plant) to the environmental concentrations. 24-h determinations of asbestos fibre concentrations in the air varied considerably, from 0.4 f/l to 4.6 f/l. The lung cancer risk due to environmental exposure of the general population to asbestos dust has been estimated to be 22 cases p.a. This seems to be very low, considering that the total number of deaths from lung cancer in Poland in 1992 was about 17.5 thousand. The environmental asbestos exposures and their health effects are limited mainly to the areas located in the vicinity of asbestos plants and are attributable primarily to improper utilization of the plant wastes (for example as the surface of local roads and sports grounds at schools) and their unathorized disposal. The incidence of pleural mesothelioma among the inhabitants of those areas seems to be endemic. The endemic character of pleural mesothelioma occurrence has been recently revealed in the vicinity of one of major Polish asbestos and cement plant.

Code(s): 6, 7.
Ding, M., X. Shi, V. Castranova and V. Vallyathan. (2000). "Predisposing factors in occupational lung cancer: inorganic minerals and chromium." J Environ Pathol Toxicol Oncol; 19(1-2):129-38 2000.
Reactive oxygen species (ROS) have been implicated in the pathogenesis of cancer. Inhalation of inorganic minerals such as asbestos and crystalline silica, and metals such as arsenic, beryllium, chromium, nickel, and vanadium, may promote directly and indirectly enhanced generation of ROS at a persistent level in concert with chronic inflammation. Perpetual ROS generation can cause specific molecular changes resulting in the activation or inactivation of transcription factors that may alter gene expression leading to cell proliferation, differentiation, and carcinogenesis. The mechanisms involved in the signal transduction leading to these processes are the subject of intense investigation. In this review, some of the recent findings from our laboratories concerning key molecular events elicited by asbestos, crystalline silica, and chromium are presented. These include genotoxicity, DNA damage, lipid peroxidation, activation of transcription factors activator protein-1 (AP-1) or nuclear factor kappa B (NF-kappaB), and p53 or k-ras gene alterations. From these studies, it is evident that ROS signaling is critical for the responses of cytokines, growth factors, and activation or inactivation of transcription factors that promote carcinogenesis.

Code(s): 6, 11.
Schneider, J., K. Rodelsperger, H. Pohlabeln and H. J. Woitowitz. (1996). "[Environmental and indoor air exposure to asbestos fiber dust as a risk and causal factor of diffuse malignant pleural mesothelioma]." Zentralbl Hyg Umweltmed. 199 (1): 1-23.
In an interdisciplinary, multicentre case control study of the causal factors of the diffuse malignant mesothelioma (DMM) standardised histories where taken from n = 324 Patients suffering from DMM, n = 315 hospital control patients (KK) and n = 182 population controls (PK). For 66 DMM, 149 KK and 107 PK a risk from asbestos fibre dust at the workplace was not detectable. For latter persons indoor and outdoor asbestos exposure outside of the workplace were investigated. The following factors were examined: neighbourhood exposure from companies using asbestos, living in big cities and nearby main traffic roads, building materials containing asbestos, electric storage heaters and household contacts. For using electric storage heaters a statistically significant increased odds ratio (OR) was observed for DMM as well in comparison with KK (OR = 2.42; 95%-CI: 1.01-5.72) and in comparison for PK (OR = 2.91; 95%-CI: 1.08-7.80). Only outside of Hamburg an increased OR compared to KK was observed for people living in the neighbourhood of asbestos factories (OR = 16.3; 95%-CI: 1.35-196.8) and also, but only in Hamburg, compared to PK living nearby main traffic roads. There is only a trend for a mesothelioma-risk for household-contacts based on a few cases. In one DMM-patient without an occupational asbestos exposure the lung dust fibre analysis yielded 2.912 FB and 1.459 x 10(3) crocydolithe fibres per gram dried lung tissue. As a child he lived in the immediate vicinity of the blue asbestos mine in Wittenoom, Australia. Therefore in special cases a para-occupational asbestos or a neighbourhood asbestos exposure can be demonstrated as a risk factor of diffuse malignant mesothelioma.

Asbestos-related, non-cancer (1, 2, 3) and cancer (4, 5, 6)
—health/irritant effects, metabolism, mechanisms

Code(s): 3, 6.
Ramanathan, A. L. and V. Subramanian. (2001). "Present status of asbestos mining and related health problems in India-- a survey." Ind Health. 39 (4): 309-15.
At present in India more than thirty mines are in operation. It produces 2800 tones of asbestos per month (mainly chrysotile and tremolite) and in recent years substantial quantity (-70%) is imported from Canada. The quality of asbestos produced in India is very poor. The mining and milling and other related processes expose the people to cancer and related diseases. Women are more affected by their exposure in processing unit compared to male who are generally working in mines. Direct and indirect employment in asbestos related industry and mine is around 100,000 workers. Latency period (length of the time between exposure and the onset of diseases) in India is estimated to be 20-37 yr. The causes for lung and breathing problem are mainly due to obsolete technology and direct contact with the asbestos products without proper precaution, because in India asbestos are sold without statutory warning. This paper reviews health effects (such as fibrosis, sequelae, bronchogenic cancer, and malignant mesothelioma) on the Indian mine workers

caused due to asbestos mining related activities with respect to their present day condition.

Code(s): 3, 6.
Levin, S. M., P. E. Kann and M. B. Lax. (2000). "Medical examination for asbestos-related disease." Am J Ind Med. 37 (1): 6-22.
There are millions of workers whose exposure to asbestos dust prior to the implementation of asbestos regulation and improved control measures places them at risk of asbestos-related disease today. In addition, workers are still being exposed to significant amounts of asbestos, when asbestos materials in place are disturbed during renovation, repair, or demolition. Given the continued presence of asbestos- containing materials in industrial, commercial, and residential settings throughout the U.S., a sizeable population remains at risk of asbestos-related disease. This article reviews the health effects associated with exposure to asbestos and delineates the steps necessary for the comprehensive screening and clinical assessment for asbestos- related disease, in order to assist physicians in identifying and preventing illness associated with exposure to asbestos among their patients.

Code(s): 3, 6.
Anonymous. (1999). "Chrysotile Asbestos." TA:NICNAS: Priority existing chemical assessment report PG:199p YR:1999 IP: VI:9.
Chrysotile, like all other asbestos forms, causes asbestosis, lung cancer and mesothelioma in humans and animals and has been shown to cause these diseases with a dose-response relationship. Chrysotile is classified as a known human carcinogen (IARC, 1987; NOHSC, 1994c). It has been shown that smoking and asbestos act in a synergistic manner, increasing the overall risk of lung cancer. There is continuing debate over the potency of chrysotile, particularly in relation to the amphiboles; crocidolite and amosite. There is accumulating evidence to indicate that chrysotile is less potent in causing asbestosis, lung cancer and mesothelioma, although this issue has not been conclusively resolved. Risk estimates are based on the incidence of lung cancer, as this is the overriding risk from asbestos exposure and insufficient dose-response data exist to estimate risks of mesothelioma. Risk estimates have assumed a linear, non-threshold approach and are extrapolated from high to low doses. Although risk estimates for chrysotile exhibit a dose-response relationship, the degree of risk appears to be dependent on the type of industry. The most relevant industry in Australia is the friction product manufacturing industry. NOHSC have estimated the risk of lung cancer in Australia based on the estimated risk in overseas friction product industries (NOHSC, 1995a). Analysis of other cohorts by US agencies provide higher risk estimates (up to 30 fold). There are many problems associated with low-dose risk extrapolation, such as the assumption of a linear relationship. However, as insufficient data exists to indicate a threshold exposure for effect, the linear extrapolation methodology provides a conservative worst-case scenario estimate of risk. Other confounding factors in estimating risks from epidemiological data are possible contamination by other fibre types and inaccurate estimates of historical exposures. Although the hazards of chrysotile (asbestosis, lung cancer and mesothelioma) have been researched and discussed in great detail, there are still many uncertainties regarding the level of risk associated with its use. Therefore, any estimate of risk should be used with caution. Chrysotile is a known human carcinogen, however the risks associated with its use are dependent on the nature of the application and of the product utilised. Based on the data available, the continued use of chrysotile on friction surfaces, gaskets, and in seals for critical industrial applications is not expected to present a significant hazard to public health. As such there are no objections to the continued use of chrysotile in these applications, however, continued progress towards a phase out of this material in favour of less hazardous materials is supported, where this phase out does not introduce greater risks through the lesser performance of substitute materials. Environment. Based on available data for Australia, it can be predicted that the use of chrysotile (including manufacturing) when used in the manners outlined in this report, will result in a low hazard to the environment. When chrysotile is encapsulated in end use products such as brake linings and epoxyresin adhesives, it is unlikely fibres will be in a form where an enviromnental hazard is posed. Therefore, disposal of used parts to standard municipal landfills is acceptable.

Code(s): 3, 6.
Germani, D., S. Belli, C. Bruno, M. Grignoli, M. Nesti, R. Pirastu and P. Comba. (1999). "Cohort mortality study of women compensated for asbestosis in Italy." American Journal of Industrial Medicine; 36 (1). 1999. 129-134.
BIOSIS COPYRIGHT: BIOL ABS. Background The carcinogenic effect of asbestos is accepted for lung cancer and mesothelioma, while conflicting opinions exist for other cancer sites. The aim of the present investigation is to study cause-specific mortality of women compensated for asbestosis who had certainly been exposed to high levels of asbestos fibers. Methods The cause-specific mortality of all Italian women compensated for asbestosis and alive December 31, 1979, was investigated through October 30, 1997. In the total coho icantly increased. Separate analyses for textile (n = 276) and asbestos-cement (n = 278) workers were performed. Women employed in the textile industry, mainly exposed to chrysotile, who are compensated at a younger age, showed higher SMRs for lung cancer and asbestosis. Women in the asbestos-cement industry, mainly exposed to crocidolite containing asbestos mixtures, experienced higher mortality for pleural malignancies. Conclusions The role of asbestos exposure in the developme

Code(s): 3, 6.
Kamp, D. W. and S. A. Weitzman. (1999). "The molecular basis of asbestos induced lung injury." Thorax; 54 (7). 1999. 638-652.
Biosis copyright: biol abs. rrm literature review human respiratory system asbestos pulmonary toxicity toxicodynamics toxin

pulmonary fibrosis pleural disease bronchogenic carcinoma malignant mesothelioma asbestosis free radical amphibole fibers inflammatory cells lung parenchymal cells reactive nitrogen species reactive oxygen species toxicology cytokines growth factors respiratory system disease neoplastic disease toxicity pathogenesis immune system respiratory system

Code(s): 3, 6.
Boffetta, P. (1998). "Health effects of asbestos exposure in humans: a quantitative assessment." Med Lav. 89 (6): 471-80.
Asbestos causes four diseases in humans: Lung fibrosis (asbestosis) follows heavy exposure and, in industrialized countries, is mainly a relic of past working conditions. The risk of pleural fibrosis and plaques is likely to be linearly dependent from time since first exposure and is present for all types of asbestos fibres. The diagnostic uncertainties regarding pleural plaques and the substantial degree of misclassification make it difficult to precisely estimate the shape of the dose-response relationship. The risk of lung cancer seems to be linearly related to cumulative asbestos exposure, with an estimated increase in risk of 1% for each fibre/ml-year of exposure. All fibre types seem to exert a similar effect on lung cancer risk; a multiplicative interaction with tobacco smoking has been suggested. Pleural mesothelioma is a malignant neoplasm which is specifically associated with asbestos exposure: the risk is linked with the cubic power of time since first exposure, after allowing for a latency period of 10 years, and depends on the fibre type, as the risk is about three times higher for amphiboles as compared to chrysotile. Environmental exposure to asbestos is also associated with mesothelioma risk.

Code(s): 3, 6.
Rosenthal, G. J., E. Corsini and P. Simeonova. (1998). "Selected New Developments in Asbestos Immunotoxicity." Environmental Health Perspectives, Vol. 106, Supplement 1, pages 159-169, 139 references, 1998.
Recent developments in studies investigating interactions of asbestos (1332214) with cells of the immune system were reviewed. The review summarized the pulmonary toxicity of asbestos and discussed recent studies investigating the effects of asbestos on nonspecific and specific immunity, and the role of iron (7439896) and reactive oxygen species in asbestos immunotoxicity. Occupational exposure to asbestos has been associated with increased risks for a range of pulmonary diseases and is considered to be an important cause of pulmonary malignancies, malignant mesothelioma and bronchiogenic carcinoma. The major disease associated with asbestos is asbestosis, which is an interstitial pulmonary fibrosis commonly thought to represent the terminal phase of a chronic inflammatory process. The inflammatory response along with peripheral immune changes following asbestos exposure has implicated the immune system in the pathogenesis of asbestos related disease. Studies investigating the effects of asbestos on nonspecific immunity have focused on the effects of exposure on natural killer (NK) cells, pulmonary macrophages, and pulmonary epithelial cells. Studies in laboratory animals have shown that asbestos impairs NK cell mediated cytotoxicity. Occupational asbestos exposure has been shown to decrease the number of circulating NK cells and to alter the number of local or interstitial NK cells in pulmonary tissues. Other studies have suggested that epithelial cells as well as macrophages and fibroblasts may be important effector cells in the immunopathogenesis of asbestos related diseases. Experimental studies and human observations have provided evidence that asbestos impairs specific mediated immunity and that these effects may be an important predisposing factor in asbestos induced fibrosis. Asbestos fibers as a result of the presence of iron on their surface may induce generation of reactive oxygen species which modulate intracellular redox states. This can contribute to the activation of transcription factors such as nuclear-factor-kappa-B and nuclear-factor-interleukin-6 which, in turn, stimulate inflammatory cytokines.

Code(s): 3, 6.
Jagirdar, J., T. C. Lee, J. Reibman, L. I. Gold, C. Aston, R. Begin and W. N. Rom. (1997). "Immunohistochemical localization of transforming growth factor beta isoforms in asbestos-related diseases." Environmental Health Perspectives; 105 (Suppl. 5). 1997. 1197-1203.
BIOSIS COPYRIGHT: BIOL ABS. Transforming growth factor beta (TGF-beta), a multifunctional cytokine and growth factor, plays a key role in scarring and fibrotic processes because of its ability to induce extracellular matrix proteins and modulate the growth and immune function of many cell types. These effects are important in inflammatory disorders with fibrosis and cancer. The asbestos-related diseases are characterized by fibrosis in the lower respiratory tract and pleura and increased occurrence of lung cancer and mesothelioma. We performed immunohistochemistry with isoform-specific antibodies to the three TGF-beta isoforms on 16 autopsy lungs from Quebec, Canada, asbestos miners and millers. There was increased immunolocalization of all three TGF-beta isoforms in the fibrotic lesions of asbestosis and pleural fibrosis. The hyperplastic type II pneumocytes contained all three isoforms. By contrast, there was differential spatial immunostaining for the TGF-beta isoforms in malignant mesothelioma

Code(s): 3, 6.
Liddell, F. D. K., A. D. McDonald and J. C. McDonald. (1997). "The 1891-1920 Birth Cohort of Quebec Chrysotile Miners and Millers: Development from 1904 and Mortality to 1992." Annals of Occupational Hygiene, Vol. 41, No. 1, pages 13-36, 30 references, 1997.
The mortality experience of male Quebec chrysotile (12001295) miners and millers was updated. The cohort included 9,780 workers

born between 1891 and 1920. Coded death certificates were used to determine cause of death. Exposure calculations were based on dust sampling, job classification, and employee and supervisor interviews. Nearly 82% of the workers were dead as of 1992. The standardized mortality ratios (SMRs), calculated in reference to the general Quebec population, were elevated for all causes for almost every decade from 1904 to 1992. Among the mine and mill workers, the SMR for cancer of the trachea, bronchus, and lung was 1.29. Among the factory workers, the SMRs for larynx cancer and for cancer of the trachea, bronchus, and lung were 2.03 and 1.34, respectively. For the 6,161 deaths which occurred after the age of 55, the SMRs for all causes and most cancers tended to increase with increasing level of exposure. For cancer of the trachea, bronchus, and lung, the SMR increased from 1.21 with less than 300 million particles per cubic foot years (mpcf.y) to 2.97 with greater than 1,000mpcf.y. Among the mill and mine workers, the rate of pneumoconiosis steadily increased with increasing exposure, from 6.95 deaths per 100,000 subject years with less than 30mpcf.y to 201.55 deaths per 100,000 subject years with greater than 1,000mpcf.y. The rate of mesothelioma tended to increase with increasing exposure, but without the same dose dependency. The overall rate of mesothelioma at the asbestos mine and mill was 13.19 deaths per 100,000 subject years. The SMRs for all causes and cancers of the trachea, bronchus, and lung increased with increasing cigarette smoking level. The authors conclude that in this cohort, the adverse health effects of chrysotile exposure are only evident at very high exposure levels.

Code(s): 3, 6.
Rahman, Q., N. Mahmood, S. G. Khan, J. M. Arif and M. Athar. (1997). "Mechanism of asbestos-mediated DNA damage: role of heme and heme proteins." Environ Health Perspect 1997 Sep;105 Suppl 5:1109-12.
Several observations, including studies from this laboratory, demonstrate that asbestos generates free radicals in the biological system that may play a role in the manifestation of asbestos-related cytotoxicity and carcinogenicity. It has also been demonstrated that iron associated with asbestos plays an important role in the asbestos-mediated generation of reactive oxygen species. Exposure to asbestos leads to degradation of heme proteins such as cytochrome P450-releasing heme in cytosol. Our simulation experiments in the presence of heme show that such asbestos-released heme may increase lipid peroxidation and can cause DNA damage. Further, heme and horseradish peroxidase (HRP) can cause extensive DNA damage in the presence of asbestos and hydrogen peroxide/organic peroxide/hydroperoxides. HRP catalyzes oxidation reactions in a manner similar to that of prostaglandin H synthetase. Iron released from asbestos is only partially responsible for DNA damage. However, our studies indicate that DNA damage mediated by asbestos in vivo may be caused by a combination of effects such as the release and participation of iron, heme, and heme moiety of prostaglandin H synthetase in free radical generation from peroxides and hydroperoxides.

Code(s): 3, 6.
Lockey, J., G. Lemasters, C. Rice, K. Hansen, L. Levin, R. Shipley, H. Spitz and J. Wiot. (1996). "Refractory ceramic fiber exposure and pleural plaques." Am J Respir Crit Care Med. 154 (5): 1405-10.
Refractory ceramic fibers (RCF) are manmade vitreous fibers (MMVF) manufactured for high-temperature applications. Between 1987 and 1992, a retrospective cohort and nested case-control study evaluated chest radiographs from 652 workers involved in the manufacture of these fibers for plausibility of a causal relationship between exposure to RCF and chest-radiographic changes. The exposure-response relationship was modeled with three variables: years since first fiber production job, years in fiber production, and cumulative fiber exposure to date of study X-ray. The case-control study used a comprehensive characterization of possible asbestos exposure to investigate asbestos as the potential causative agent of chest-radiographic changes. Chest radiographs of 20 workers (3.1%) demonstrated 19 pleural plaques and one diffuse pleural thickening. Nine of 72 workers (12.5%) with more than 20 yr since their first fiber-production job had plaques (odds ratio [OR] = 9.5; 95% confidence interval [CI] = 1.9 to 48.2). Five of 19 workers with more than 20 yr in fiber-production work (26.3%) had plaques (OR = 22.3; 95% CI = 3.6 to 137.0). Similarly, adjusted ORs demonstrated a progressive relationship between cumulative fiber-months per milliliter (fiber-mo/ml) exposure and plaques. The case-control study confirmed that asbestos exposure did not account for the observed association between fiber exposure and plaques. A validity review of historical films demonstrated biologic plausibility for the association, since sufficient latency existed from the time of first RCF exposure to the development of plaques. There was no significant increase in parenchymal changes consistent with interstitial fibrosis.

Code(s): 3, 6.
Schneider, J., K. Straif and H. J. Woitowitz. (1996). "Pleural mesothelioma and household asbestos exposure." Rev Environ Health. 11 (1-2): 65-70.
This article discusses the development of asbestos-induced malignant mesotheliomas after non-occupational environmental exposure to asbestos through contact with occupationally exposed household members. In our policlinic, we have seen six fatal pleural mesothelioma cases (five wives and one son of asbestos-industry workers) with no history of occupational asbestos exposure. In five women, a causal relation was established between the fatal disease and inhalation of asbestos fibers while cleaning the contaminated work-clothes and shoes of their husbands at home. The son had also been exposed to asbestos throughout his childhood during daily visits with his father at the workplace.

Code(s): 3, 6.
Morgan, A. (1995). "Deposition of inhaled asbestos and man-made mineral fibres in the respiratory tract." Ann Occup Hyg. 39 (5): 747-58.
This paper reviews publications dealing with the deposition of fibrous particles, including asbestos and man-made mineral fibres, in the respiratory tract of man and experimental animals, particularly of the rat. The effects of fibre diameter and length on total, thoracic and alveolar deposition are discussed. Total deposition in the respiratory tract of the rat increases quite steeply with aerodynamic diameter (Dae) from about 20% at a Dae of 1 micron to 100% at a Dae of 5 microns. Deposition in the alveolar region reaches a peak of about 10% at a Dae of about 2 microns, which corresponds to an actual fibre diameter of about 0.4 microns. For fibres with diameters greater than this, alveolar deposition falls rapidly. For example, long glass fibres with an actual diameter of 1.5 microns or short glass fibres with an actual diameter of 3 microns are essentially non-respirable in the rat. The fate of fibres deposited in different regions of the respiratory tract of the rat is also discussed and the factors which predispose fibres either to remain in alveolar macrophages or to be transferred to the interstitium and pulmonary lymphatics. Finally, the distributions in the lungs of fibres administered by inhalation and by intratracheal instillation are compared, and the advantages and drawbacks of each method of delivery discussed.

Code(s): 3, 6, 7, 8, 9.
Brown, D. M., C. Fisher and K. Donaldson. (1998). "Free radical activity of synthetic vitreous fibers: iron chelation inhibits hydroxyl radical generation by refractory ceramic fiber." J Toxicol Environ Health A. 53 (7): 545-61.
Synthetic vitreous fibers are in widespread use but the parameters that dictate their carcinogenicity are still a matter of scientific debate. The free radical activities of a panel comprising an asbestos sample and five different respirable synthetic vitreous fiber samples were determined, to address the hypothesis that carcinogenic fibers have greater free radical activity than noncarcinogenic fibers. On the basis of recent inhalation studies, the six samples were divided into three carcinogenic fibers-amphibole asbestos, silicon carbide, and refractory ceramic fiber 1 (designated with the abbreviation RCF 1)-and three noncarcinogenic fibers--man-made vitreous fiber 10 (a glass fiber sample designated with the abbreviation MMVF 10), Code 100/475 glass fiber, and RCF4. All experiments were carried out with equal fiber numbers. Of the two assays of free radical activity used, the plasmid assay of DNA scission showed only amosite asbestos to have free radical activity, while the salicylate assay of hydroxyl activity showed that both amosite asbestos and RCF1 release hydroxyl radicals; silicon carbide fibers had no free radical activity in either of the assays. None of the noncarcinogenic fibers demonstrated free radical activity in either of the assays. The differences in the two assays in demonstrating free radical activity with RCF1 may be due to increased release of Fe from RCF1 under the more acid conditions of the salicylate assay, which was confirmed by the fact that soluble iron caused hydroxylation of salicylate. Presence of an iron chelator inhibited the ability of the RCF1 fibers to cause hydroxylation of salicylate, demonstrating that RCF1 generates hydroxyl radical by Fenton chemical reaction in the same way as amphibole asbestos.

Code(s): 3, 6, 14.
Mendes, R. (2001). "[Asbestos and disease: review of the scientific knowledge and a rationale for urgent change in the current Brazilian policy about this question]." Cad Saude Publica. 17 (1): 7-29.
This paper is a state-of-the-art review of scientific knowledge on both the health effects of asbestos fiber inhalation and possibilities for safe and sustainable prevention, from an ethical, political, and technological point of view. The author provides scientific background and arguments from the ongoing discussion in Brazil concerning the need to redefine current asbestos policy, in order to establish a more advanced and appropriate policy whose priority is the protection of life, human health, and the environment. The first part deals with several technological and economic aspects of asbestos-chrysotile. In the second part, the author presents and discusses a bibliographic review of the construction of scientific knowledge on the health effects of asbestos fibers, first within an international perspective, and then (in the third part), from a Brazilian view. The fourth part analyzes the current debate on the fibrogenicity and carcinogenicity of asbestos-chrysotile. Some current responses from the international community towards the asbestos-chrysotile ban are also discussed. Finally, the author discusses the historical inadequacy of Brazilian asbestos policy and the urgent need to revise it to include a ban on asbestos-chrysotile in this country.

Code(s): 3, 6, 14.
Wozniak, H. and E. Wiecek. (1996). "Asbestos and Asbestos-Related Diseases." Annals of Agricultural and Environmental Medicine, Vol. 3, No. 1, pages 1-8, 104 references, 1996.
The mineralogy, physical and chemical properties and health effects (asbestosis, pleural plaques, cancers, mesothelioma) of asbestos (1332214) were reviewed. Asbestos is used primarily in products in which it is incorporated into matrices. The asbestos cement industry is the largest user of asbestos fibers worldwide, accounting for some 85% of all asbestos in use today. Facilities to make asbestos cement exist in more than 100 countries, manufacturing 27 to 30 million tons of product each year. The asbestos cement products contain 10 to 15% of asbestos, mostly chrysotile (12001295), although limited amounts of crocidolite (12001284) have been used in large pipes. It is estimated that around 10,000 workers were occupationally exposed to asbestos in Poland which used to be

ranked high among the world producers and consumers of asbestos goods. About 65% of the asbestos there was used to make asbestos cement products in seven industrial facilities. The risk of lung cancer related to asbestos exposure may be greater in the textile industry than in mining and milling, or in the manufacture of friction products such as break pads and linings. The incidence of mesothelioma has traditionally be high among insulation workers, those who work in asbestos facilities and those who work in shipyards.

Code(s): 3, 6, 14.
Seaton, A. (1995). "[Asbestos: past, present and future]." Schweiz Med Wochenschr. 125 (10): 453-7.
Owing to its particular properties asbestos has been widely used for the production of insulating material, for fire proofing, and for strengthening to other materials such as cements and plastics, and thus the story of this mineral was one of progressive commercial success until the middle of this century. However, serious health hazards were realized early: around the turn of the century a progressive form of diffuse fibrosis (asbestosis) in asbestos workers was observed and in 1950 an excess risk of lung cancer, while in 1960 the causal relationship between asbestos and mesothelioma were confirmed. In view of the known potential risks of asbestos and its widespread use in the building industry, more recently asbestos has caused considerable public concern and anxiety. Based on numerous experimental and epidemiological observations, present knowledge of the pathogenic effects of asbestos is sufficient for a number of broad conclusions to be drawn. (1) The amphibole types of asbestos are too dangerous for use as industrial material, and should be banned. (2) Chrysotile can probably be used safely if there is strict control of the workers' dust exposure. (3) It is very unlikely that the general public is at any measurable risk from asbestos in buildings. Exceptions are people working regularly on maintenance tasks involving removing or cutting of asbestos in buildings; such people are properly classified as asbestos workers and should be protected accordingly.(ABSTRACT TRUNCATED AT 250 WORDS)

Asbestos and Man-made Vitreous Fibers (MMVFs), other (7)
—pulmonary depositional patterns, biopersistence, miscellaneous of potential relevance

Code(s): 7.
Ruotsalainen, M., M. R. Hirvonen, K. Luoto and K. M. Savolainen. (1999). "Production of reactive oxygen species by man-made vitreous fibres in human polymorphonuclear leukocytes." Hum Exp Toxicol. 18 (6): 354-62.
Human polymorphonuclear leukocytes (PMNL) or erythrocytes, isolated from human blood, were exposed to graded doses of asbestos (chrysotile), quartz, or man-made vitreous fibres (MMVF), i.e. refractory ceramic fibres (RCF), glasswool, or rockwool fibres. None of the MMVF affected either the viability of PMNL, as measured by trypan blue exclusion test, or induced haemolysis, whereas the positive controls, quartz and chrysotile, dose-dependently induced haemolysis in PMNL. MMVF did not increase the release of lactate dehydrogenase (LDH) from the PMNL, whereas the positive controls, chrysotile and quartz, induced a marked and dose-dependent release of LDH. When PMNL were exposed to MMVF, some of the fibre types slightly increased the levels of free intracellular calcium ([Ca2+]i) within the cells in a manner similar to that induced by chrysotile or quartz. All MMVF induced a dose-dependent production of reactive oxygen species (ROS) in PMNL, with RCF-induced production of ROS being the most marked. Production of ROS by MMVF seemed to depend on the availability of extracellular calcium because it could be attenuated with a Ca2+ channel blocker, verapamil, or a Ca2+ chelating agent, EGTA. Production of ROS may be a common pathway through which PMNL respond to MMVF-induced cell activation, but alterations of levels of free intracellular Ca2+ do not seem to be an absolute prerequisite for this effect. Fibre length seemed not to be an important factor in affecting the ability of MMVF to induce ROS production in PMNL. However, the balance between different elements in the fibre seemed importantly to affect the biological activity of a fibre.

Code(s): 7.
Guldberg, M., V. R. Christensen, M. Perander, B. Zoitos, A. R. Koenig and K. Sebastians. (1998). "Measurement of in-vitro fibre dissolution rate at acidic pH." Annals of Occupational Hygiene; 42 (2). 1998. 233-243.
BIOSIS COPYRIGHT: BIOL ABS. A low biopersistence of man-made vitreous fibres (MMVFs) has often been related to a high in-vitro dissolution rate at near-neutral pH. For some fibre types, however, a low in-vivo biopersistence cannot be explained by the in-vitro dissolution rate in near-neutral physiological fluids. It has been suggested, that the high in-vitro dissolution rate of these fibres at the acidic pH which is found inside the phagolysosomes of the alveolar macrophages could be the reason for the fast in-vivo clearance of such fibres. The aim of this study was, through interlaboratory comparison of in-vitro dissolution measurements at acidic pH, to investigate the causes of variations and to identify key parameters for a measurement method similar to the method used at near neutral pH. Results of in-vitro measurements of different fibre types at acidic pH are presented, and the influence of different test parameters described. The measurements and calculations at acidic pH can be made simila

Code(s): 7.
Beswick, P. H. (1997). "Free Radical Activity of Industrial Fibers: Role of Iron inOxidative Stress and Activation of Transcription Factors." Environ Health Perspect. 105S (Suppl 5): 1313-7.
We studied asbestos, vitreous fiber (MMVF10), and refractoryceramic fiber (RCF1) from the Thermal Insulation Manufacturers'

Associationfiber repository regarding the following: free radical damage to plasmidDNA, iron release, ability to deplete glutathione (GSH), and activateredox-sensitive transcription factors in macrophages. Asbestos had muchmore free radical activity than any of the man-made vitreous fibers. MoreFe3+ was released than Fe2+ and more of both wasreleased at pH 4.5 than at pH 7.2. Release of iron from the differentfibers was generally not a good correlate of ability to cause free radicalinjury to the plasmid DNA. All fiber types caused some degree of oxidativestress, as revealed by depletion of intracellular GSH. Amosite asbestosupregulated nuclear binding of activator protein 1 transcription factor toa greater level than MMVF10 and RCF1; long-fiber amosite was the only fiberto enhance activation of the transcription factor nuclear factor [kappa]B(NF[kappa]B). The use of cysteine methyl ester and buthionine sulfoximineto modulate GSH suggested that GSH homeostasis was important in leading toactivation of transcription factors. We conclude that the intrinsic freeradical activity is the major determinant of transcription factoractivation and therefore gene expression in alveolar macrophages. Althoughthis was not related to iron release or ability to deplete macrophage GSHat 4 hr, GSH does play a role in activation of NF[kappa]B.

Code(s): 7.
Golladay, S. A., S. H. Park and A. E. Aust. (1997). "Efflux of Reduced Glutathione after Exposure of Human Lung Epithelial Cells to Crocidolite Asbestos." Environmental Health Perspectives, Vol. 105, Supplement 5, pages 1273-1277, 37 references, 1997.
The effects of crocidolite (12001284) on glutathione homeostasis was studied in human lung cells. Human lung epithelial cells (A549) were incubated with 3 micrograms per square centimeter (microg/cm2) crocidolite fibers or crocidolite from which the iron had been removed by pretreatment with desferrioxamine-B (DF/crocidolite) for 24 hours. The effects on intracellular reduced-glutathione (GSH), oxidized-glutathione (GSSG), glutathione/protein mixed disulfides (GPMDS), glutathione conjugates, gamma-glutamyl-cysteine-synthetase (gGCS), glutathione-reductase (GRe), glutathione-peroxidase (GPx), glucose-6-phosphate-dehydrogenase (G6PDH), and S-nitroso-thiol levels were determined. Release of intracellular lactate-dehydrogenase (LDH) activity or carbon-14 (C14) activity from cells that had been preloaded with C14 labeled adenine into the extracellular medium was measured as a marker of cellular membrane damage. Samples were withdrawn periodically to measure changes in intracellular/extracellular glutathione. Incubation with crocidolite for 24 hours caused a 59% decrease in intracellular GSH levels without affecting GSSG levels. Treatment with DF/crocidolite caused a similar decrease in intracellular GSH content, suggesting that the GSH depletion was not caused by iron catalyzed reactions. Increased formation of S-nitrosothiols also occurred. This increase was blocked by DF/crocidolite. Neither form of crocidolite altered the concentrations of GPMDS nor glutathione conjugates. Activity of gGCS was decreased by 47% by both forms of crocidolite. GRE, GPx, GST, and G6PDH activities were unaffected. No increased leakage of LDH or adenine derived C14 activity into the medium was detected, indicating GSH decreases were not due to membrane damage. Crocidolite caused time dependent decreases in intracellular total glutathione and GSH levels starting after 4 hours. The GSSG level remained constant. Concentrations of total glutathione in the medium increased during incubation, reaching 50% of the total by 24 hours. The halflife of GSH in the medium was less than 1 hour, suggesting GSH was released continuously by cells into the medium during exposure. The authors conclude that exposure of A549 cells to crocidolite causes efflux of intracellular GSH into the extracellular medium, formation of S-nitrosothiols, and decreases gGCS activity.

Code(s): 7.
Hippeli, S., K. Dornisch, S. Kaiser, U. Drager and E. F. Elstner. (1997). "Biological Durability and Oxidative Potential of a Stonewool Mineral Fibre Compared to Crocidolite Asbestos Fibres." Archives of Toxicology, Vol. 71, No. 8, pages 532-535, 12 references, 1997
AB - The oxidative potentials of a stonewool mineral fiber (SWMF) and crocidolite (12001284) fibers were evaluated and compared. A man made vitreous fiber (stonewool-number-13) with a relatively low aluminum-oxide content and a high calcium-oxide content, and crocidolite fibers at concentrations of 4mg/ml were incubated in Gamble solution (GS), a solution simulating deproteinated plasma and a surfactant like solution (SLS), prepared by adding ethanolic phosphatidylcholine to GS, for up to 16 weeks (wk) at 37 degrees-C. The reactions were run at pH 5.5 and 7.4. Aliquots of the incubation mixtures were removed at weekly intervals. The oxidative potential of the samples was assessed by addition to alpha-keto-gamma-methiol-butyric-acid (KMB) in a NADH/butyric-acid/ethylenediaminetetraacetic-acid system and measuring the extent of formation of reactive oxygen species from measurements of the amounts of ethylene released from the KMB by gas chromatography. Crocidolite demonstrated significantly greater oxidative reactivity than the SWMF at all time points in both GS and SLS. The oxidative potential of both fiber types was not constant over time, but showed sinusoidal like fluctuations, which at times showed much greater reactivity than at the start of incubation. The level of reactivity of both fibers was generally lower in SLS than in GS. The oxidative potential of the SWMF in SLS disappeared by the end of the incubation period. The oxidative potential of the SWMF was not affected by pH. The oxidative potential of crocidolite was much higher at pH 5.5 in both media compared to pH 7.4. The authors conclude that under the experimental conditions, crocidolite has demonstrated a much higher oxidative potential than the SWMF, although both fibers showed changes in reactivity over the incubation period. Continuous measurements of oxidative potential should provide a better indication of fiber biodurability than measures of changes in fiber number, mass, or distributions in fiber length.

Code(s): 7.

Muhle, H. and B. Bellmann. (1997). "Significance of the biodurability of man-made vitreous fibers to risk assessment." Environ Health Perspect. 105 Suppl 5 1045-7.
It is generally agreed that the biodurability of man-made vitreous fibers is a major factor for the characterization of potential health effects. As there is currently no standardization of experimental protocols to determine biodurabilty, the results of the clearance assays have not been used up to now for regulatory purposes. Methods used to analyze biodurability in animal models are short-term inhalational exposure and intratracheal instillation of rat respirable fibers. Both test methods have strengths and limitations for regulatory purposes. We outline recommended procedures for standardized biodurability assays that can be used to compare different fiber types. In animal experiments, biodurability is difficult to separate from biopersistence, as mucociliary and macrophage-mediated clearance occur simultaneously with dissolution and disintegration. For intratracheal instillation, a sized rat respirable sample must be used. Precautions should be taken to prevent aggregation of fibers in the lungs. Although from a scientific point of view questions remain about quantifying the influence of fiber length, diameter, dose, and exposure route, consistent data on the biodurability of vitreous glass fibers are available which may be used for regulatory purposes.

Code(s): 7.
Donaldson, K., P. H. Beswick and P. S. Gilmour. (1996). "Free radical activity associated with the surface of particles: a unifying factor in determining biological activity?" Toxicol Lett 1996 Nov;88(1-3):293-8.
Using a sensitive phi X174 RF plasmid DNA assay, free radical activity was detected at the surface of normal and ultrafine titanium dioxide (TiO2), environmental particles (PM-10), asbestos and a range of man-made fibres. There were differences in the amount of free radical activity that was detected, with ultrafine TiO2 being much more active than normal-sized TiO2; PM-10 also had substantial free radical activity. Amphibole asbestos samples were highly active, whilst man-made fibres were much less active than asbestos. For all of the particles, the DNA damage could be ameliorated by mannitol, showing that hydroxyl radicals were involved. The ability of particles to generate free radicals at or near their surface, and thereby impose oxidant stress in key target cells, could be central to determining their pathogenicity.

Code(s): 7.
Gelzleichter, T. R., E. Bermudez, J. B. Mangum, B. A. Wong, J. I. Everitt and O. R. Moss. (1996). "Pulmonary and pleural responses in Fischer 344 rats following short- term inhalation of a synthetic vitreous fiber. I. Quantitation of lung and pleural fiber burdens." Fundam Appl Toxicol. 30 (1): 31-8.
The pleura is an important target tissue of fiber-induced disease, although it is not known whether fibers must be in direct contact with pleural cells to exert pathologic effects. In the present study, we determined the kinetics of fiber movement into pleural tissues of rats following inhalation of RCF-1, a ceramic fiber previously shown to induce neoplasms in the lung and pleura of rats. Male Fischer 344 rats were exposed by nose-only inhalation to RCF-1 at 89 mg/m3 (2645 WHO fibers/cc), 6 hr/day for 5 consecutive days. On Days 5 and 32, thoracic tissues were analyzed to determine pulmonary and pleural fiber burdens. Mean fiber counts were 22 x 10(6)/lung (25 x 10(3)/pleura) at Day 5 and 18 x 10(6)/lung (16 x 10(3)/pleura) at Day 32. Similar geometric mean lengths (GML) and diameters (GMD) of pulmonary fiber burdens were observed at both time points. Values were 5 microns for GML (geometric standard deviation GSD approximately 2.3) and 0.3 micron for GMD (GSD approximately 1.9), with correlations between length and diameter (tau) of 0.2-0.3. Size distributions of pleural fiber burdens at both time points were approximately 1.5 microns GML (GSD approximately 2.0) and 0.09 micron GMD (GSD approximately 1.5; tau approximately 0.2-0.5). Few fibers longer than 5 microns were observed at either time point. These findings demonstrate that fibers can rapidly translocate to pleural tissues. However, only short, thin (< 5 microns in length) fibers could be detected over the 32-day time course of the experiment.

Code(s): 7.
Luoto, K., M. Holopainen, M. Perander, K. Karppinen and K. M. Savolainen. (1996). "Cellular effects of particles--impact of dissolution on toxicity of man- made mineral fibers." Cent Eur J Public Health. 4 (Suppl): 29-32.
The use of man-made vitreous fibers (MMVF) has grown rapidly because exposure to natural fibers, mainly asbestos, has proved harmful to humans. Biological activity of MMVF made of glass, rock, slag, or other minerals does not depend only on their respirability, but also on their chemical durability and persistency. In the use of MMVF, the goal is to decrease harmful effects of fibers by increasing their dissolution and removal from the lungs. The dissolution of Fe and Al from MMVF is more marked by rat alveolar macrophages (AMs) in culture than by mere medium, whereas medium is more effective than AMs in dissoluting silicon (Si) from MMVF, Fe and Al content of the fibers correlate negatively with the fiber Si dissolution by the AMs. Scanning electron micrographs show that MMVF are readily phagocytized by rat AMs in culture. The phagocytosis begins within 30 min after the onset of the exposure and continues for a 96-h observation period. Short fibers, less than 20 microns in length, are readily phagocytized by the AMs whereas longer fibers are attacked with a large number of AMs. MMVF induce also non-lethal changes in the rat AM surface morphology. Before exposure the cells have continuous membranes. The exposed AMs produce extensions which fasten them to the fibers or to other cells to form clumps or clusters of cells and fibers, each cell engulfing a part of a fiber. Over 70% of the exposed cells are viable after 96 h of exposure suggesting that MMVF are not acutely toxic rat AMs. MMVF also slightly damage cell

membrane and increase the production of reactive oxygen species.

Code(s): 7.
Treadwell, M. D., B. T. Mossman and A. Barchowsky. (1996). "Increased neutrophil adherence to endothelial cells exposed to asbestos." Toxicology and Applied Pharmacology; 139 (1). 1996. 62-70.
BIOSIS COPYRIGHT: BIOL ABS. Inhalation of asbestos may activate the pulmonary endothelium to promote an inflammatory cell phenotype that participates in the development of pulmonary fibrosis. However, little is known about the effects of asbestos on endothelial cell function. Therefore, endothelial cells were exposed to chrysotile and crocidolite asbestos for up to 72 hr to investigate the effects of noncytotoxic concentrations of asbestos on cell function. Noncytolytic concentrations of chrysotile and crocidolite caused localized changes in cell morphology, resulting in activation of endothelial cells to a vacuolated, "spindle-shaped" morphology at sites of fiber deposition. The adherence of neutrophils (PMN) to control and asbestos-treated cultures was examined to determine the functional significance of this altered morphology. Chrysotile asbestos caused a time-dependent, 2- to 4-fold increase in PMN adherence that was localized to spindled endothelial cells in close contact with fibers. Monocl

Code(s): 7.
Eastes, W., K. J. Morris, A. Morgan, K. A. Launder, C. G. Collier, J. A. Davis, S. M. Mattson and J. G. Hadley. (1995). "Dissolution of Glass Fibers in the Rat Lung following Intratracheal Instillation." Inhalation Toxicology, Vol. 7, No. 2, pages 197-213, 16 references, 1995.
The dissolution rate of glass fibers was measured in simulated lung fluid at neutral pH and compared with measurements in rat lung. Glass fibers of five different compositions were instilled intratracheally in female Fischer-344-rats. The fibers had dissolution rates of 2, 100, 150, 300, and 600 nanograms/centimeter squared/hour. Rats were sacrificed at various times up to 1 year after exposure. For fibers longer than 20 microns, peak diameter decreased steadily until it reached 0.3 microns. Agreement between in-vivo and in-vitro measurements was excellent. Dissolution of long fibers proceeded by reducing fiber diameter steadily until fibers disappeared. Dissolution occurred for a wide range of fibers, including those that dissolved in 1 month and those that took several years to dissolve. Macrophage mediated clearance of short fibers did not operate after intratracheal instillation. The ratio of the number of long fibers to the number of short fibers remaining in rat lungs showed that slowly dissolving fibers remained constant for 1 year, whereas long fibers disappeared rapidly. This ratio was confirmed by computer simulation and measuring fibers in lungs. Fiber breakage was not observed. The authors conclude that dissolution, not breakage, is the main contributor to the elimination of long fibers.

Code(s): 7.
Leanderson, P. and W. Sahle. (1995). "Formation of Hydroxyl Radicals and Toxicity of Tungsten Oxide Fibres." Toxicology in Vitro; 9 (2). 1995. 175-183.
BIOSIS COPYRIGHT: BIOL ABS. Occupational exposure to hard metal dust may cause interstitial pulmonary fibrosis and asthma. The cause of asthma is well established, whereas the cause of lung fibrosis is still under debate. Recently, slightly reduced airborne tungsten oxide fibres, the role of which in hard metal pneumoconiosis has never been accounted for, were detected in an air sample from a hard metal production plant. In this study, the capacity to generate hydroxyl radicals, toxicity to cultured human lung cells and haemolytic activity of tungsten oxide fibres were compared with crocidolite asbestos fibres. The results show (a) that tungsten oxide fibres can generate hydroxyl radicals, and (b) that tungsten oxide fibres were more cytotoxic to human lung cells than was crocidolite, but (c) that the haemolytic activity of tungsten oxide fibres was lower than for crocidolite.

Code(s): 7.
Pelin, K., A. Hirvonen, M. Taavitsainen and K. Linnainmaa. (1995). "Cytogenetic response to asbestos fibers in cultured human primary mesothelial cells from 10 different donors." Mutat Res 1995 Apr;334(2):225-33.
The ability of amosite asbestos fibers to induce chromosomal aberrations in human primary mesothelial cells obtained from pleural effusions of 10 noncancerous patients was investigated. The glutathione S-transferase M1 (GSTM1) genotypes of the patients were determined, since the GSTM1 null genotype has been associated with increased susceptibility to lung cancer and chemically induced cytogenetic damage. Four of the patients represented the GSTM1 null genotype, and six the GSTM1 positive genotype. Successful chromosome aberration analyses were obtained from six cases, three of them with the GSTM1 null genotype. The level of aberrant cells in unexposed cultures ranged from 2.0% to 7.5%. Statistically significant increases (2.3-3.0-fold compared to controls) in the number of aberrant cells were observed in two cases only: in one case treated with 1 microgram/cm2 of amosite, and in another treated with 2 micrograms/cm2 of amosite. Cell cultures from four individuals showed minor or no increases in the numbers of aberrant cells in the doses tested (1 and 2 micrograms/cm2). Chromosome breaks were the major type of aberration. The amosite exposed cells with significantly increased aberrations were from patients with GSTM1 positive genotypes. Two cases that showed no cytogenetic response to asbestos fibers were of the GSTM1 null genotype. Thus, our results suggest that the lack of the GSTM1 gene does not render human mesothelial cells more susceptible to chromosomal damage induced by asbestos. GSTM1 null cells appeared, however, to be more sensitive to the growth inhibitory effects of asbestos than did GSTM1 positive cells. Variation in the cytogenetic response

of human primary mesothelial cells to asbestos fibers was observed to exist, but the fibers do not appear to be potent inducers of structural chromosomal aberrations in these cells. It remains to be established whether individual sensitivity to asbestos fibers, due to specific genetic traits, exists.

Man-made Vitreous Fibers (MMVFs), non-cancer (8, 10)
—health/irritant effects, metabolism, mechanisms

Code(s): 8.
Guldberg, M., S. L. Jensen, T. Knudsen, T. Steenberg and O. Kamstrup. (2002). "High-Alumina Low-Silica HT Stone Wool Fibers: A Chemical Compositional Range with High Biosolubility." Regul Toxicol Pharmacol. 35 (2 Pt 1): 217-26.
Man-made vitreous fibers (MMVF) are classified within the European Union (EU) as carcinogenic category 3 (possibly carcinogenic), but criteria exist to exonerate fibers from this classification. The HT stone wool fiber type is a MMVF that fulfills European regulatory requirements for exoneration from classification as a carcinogen based on in vivo testing. The chemical composition of the fibers and the results of the in vivo and in vitro studies that defined the chemical compositional range for a CAS registry number for these fibers are presented and discussed. Results from in vitro dissolution measurements at pH 4.5 of 52 fiber compositions (9-23 wt% Al(2)O(3) and 32-47 wt% SiO(2)) ranging from traditional stone wool to the biosoluble HT fibers are presented. The results are evaluated as a function of the ratio Al/(Al+Si) in the glass network and as a function of the fraction of Si- O-Si linkages in the glass. It is suggested that the dissolution mechanism for these fibers relates to the density of the surface silica layer on dissolving fibers and that the fraction of Si-O-Si linkages influences this. (c) 2002 Elsevier Science (USA).

Code(s): 8.
Hesterberg, T. W., G. A. Hart, W. C. Miiller, G. Chase, R. A. Rogers, J. B. Mangum and J. I. Everitt. (2002). "Use of short-term assays to evaluate the potential toxicity of two new biosoluble glasswool fibers." Inhal Toxicol. 14 (3): 217-46.
Two new glasswools were developed for optimal biosolubility in the lung: JM 902, for insulation and filtration; and JM 901F, for standard thermal and acoustical insulation. Both were tested for lung biopersistence and their potential to induce persistent pulmonary inflammation in rats. Their dissolution rate constants (k(dis)) were estimated in vitro. Results for 902 were: in vitro k(dis) (pH 7.4) = 150 ng/cm2/h; after 5 days of fiber inhalation (IH), lung clearance of fibers > 20 microm length (F > 20 microm) indicated a weighted half- time (WT(1/2)) of 6.8 days and 90% clearance time (T90) of 33 days; following intratracheal instillation (IT), lung clearance half-time (T(1/2)) for F > 5 microm was 20 days. Results for 901F were: k(dis) (pH 7.4) = 500-560; after 5 days of fiber inhalation exposure, WT(1/2) (F > 20 microm) = 8.1 days and T90 = 38 days. After 5 days of fiber inhalation, both fibers induced initial pulmonary inflammation followed by return to normal within 3 wk postexposure. Lung clearance half-times for 902 and 901F passed the European Union (EU) criteria for noncarcinogenic fibers (IH WT(1/2) F > 20 microm was < 10 days); 902 passed the noncarcinogenic criterion of the German government (IT T(1/2) F > 5 microm was < 45 days). Thus, carcinogenicity labeling is not required for either fiber in the EU. Short-term test results for 902 and 901F were similar to results for synthetic vitreous fibers (SVFs) that were innocuous in rodent chronic inhalation studies, but short-term test results for 902 and 901F differed sharply from results for other SVFs that were pathogenic in chronic studies. Thus, these short-term tests indicate that 902 and 901F are biosoluble fibers and would be nonpathogenic in the rat exposed by inhalation.

Code(s): 8.
Lockey, J. E., G. K. LeMasters, L. Levin, C. Rice, J. Yiin, S. Reutman and D. Papes. (2002). "A longitudinal study of chest radiographic changes of workers in the refractory ceramic fiber industry." Chest. 121 (6): 2044-51.
STUDY OBJECTIVE: This industry-wide longitudinal study examines chest radiographic changes of workers manufacturing refractory ceramic fibers (RCF). DESIGN: Chest radiographs were obtained every 3 years and were interpreted using the 1980 International Labour Organization classification for pneumoconiosis. Three exposure metrics were calculated: duration and latency in a production job, and cumulative exposure (fiber-months per cubic centimeter). PARTICIPANTS: The radiographic survey included 625 current workers at five manufacturing sites and 383 former workers at two of the five sites. MEASUREMENTS AND RESULTS: Pleural changes were seen in 27 workers (2.7%). Of workers with > 20 years of latency from initial production job or 20 years of duration in a production job, 16 workers (8.0%) and 5 workers (8.1%) demonstrated pleural changes, respectively. Results from the cumulative exposure analysis (> 135 fiber-months per cubic centimeter) demonstrated a significant elevated odds ratio (OR) of 6.0 (95% confidence interval [CI], 1.4 to 31.0). The incidence of irregular opacities at profusion categories > or = 1/0 was similar to other nonspecified dust-exposed worker populations at 1.0%, and showed a nonsignificant elevated OR in regard to cumulative fiber exposure of 4.7 (95% CI, 0.97 to 23.5). CONCLUSIONS: RCF are significantly associated with pleural changes that were predominantly pleural plaques, but have not resulted in a statistically significant increase in interstitial changes.

Code(s): 8.
Kim, K. A., W. K. Lee, J. K. Kim, M. S. Seo, Y. Lim, K. H. Lee, G. Chae, S. H. Lee and Y. Chung. (2001). "Mechanism of refractory

ceramic fiber- and rock wool-induced cytotoxicity in alveolar macrophages." Int Arch Occup Environ Health. 74 (1): 9-15.
OBJECTIVES: Man-made vitreous fibers (MMVFs) can induce cytotoxicity in a way similar to that of other particles, including silica and asbestos fibers. However, as yet the mechanism of MMVF-induced cytotoxicity is still not clear. This report aims to clarify the mechanism of MMVF- induced cytotoxicity in the alveolar macrophage (AM). In this mechanism, an attempt to prove the involvement of the adenosine triphosphate (ATP) generation system and the polyinosinic acid- inhibitable scavenger receptors was made. METHODS: Several parameters were observed for cytotoxicity, such as cell viability, the release of lactic dehydrogenase (LDH) and ATP levels in rat AM's that were treated with refractory ceramic fibers (RF2) and rock wool (RW1). A specially designed ATP generation system was used to determine the effect of MMVF on ATP generation. A scavenger receptor ligand was applied to evaluate the relationship between scavenger receptors and MMVF-induced ATP depletion. RESULTS: A 3-(4,5-dimethylthiazol)-2,5-diphenyl tetrazolium bromide (MTT) assay indicated that both RF2 and RW1 caused a decrease in cell viability and this decrease was concentration-dependent. RF2 and RW1 increased the release of LDH with increasing fiber concentration. From these parameters, RF2 was shown to exhibit greater cytotoxicity than did RW1. Both fibers decreased the intracellular ATP content and this decrease was concentration-dependent. The decrease was more pronounced in RW1 than in RF2 at all fiber concentrations. These fibers suppressed succinate-triggered oxygen consumption. Polyinosinic acid, a ligand of the scavenger receptor, inhibited the MMVF-induced decrease in ATP concentration. CONCLUSION: These results suggest that RF2 and RW1 can induce cytotoxicity and ATP depletion in the AM through the polyinosinic acid-inhibitable scavenger receptor. ATP depletion was the important factor in MMVF cytotoxicity, especially by RW1.

Code(s): 8.
Kiec-Swierczynska, M. and J. Wojtczak. (2000). "Occupational ceramic fibres dermatitis in Poland." Occup Med (Lond). 50 (5): 337-42.
Recently, the use of asbestos has been considerably limited in Poland, with the simultaneous increase in the manufacture, processing and application of man-made mineral fibres, which includes ceramic fibres. The aims of this study were (1) to assess the type and frequency of dermal changes caused by the irritant activity of ceramic fibres among workers at the plants that manufacture packing and insulation products; and (2) to compare the irritant activity of Polish-made L-2 and L-3 ceramic fibres with that of the Thermowool ceramic fibres made in England. Workers (n = 226) who were exposed to ceramic fibres underwent dermatological examination. Patch tests with the standard allergen set, together with samples of the fibres L-2, L-3, and Thermowool fibres, were applied to all the workers. It has been shown that the Polish-made L-2 and L-3 fibres differed from Thermowool fibres in that the L-2 and L-3 fibres contained zirconium and were coarser. The proportion of filaments with diameters above 3 microns was 11.1% in the L-3 fibre and 6.3% in the L-2 fibre samples. The Thermowool fibre did not contain filaments thicker than 3 microns. Evident dermal changes, resulting from strong irritant activity of the fibres, were detected in 109 (48.2%) of the workers examined. Irritant contact dermatitis acuta (maculae, sometimes papulae and small crusts on the upper extremities, trunk, and lower extremities), disappearing after 2-3 days, was found in 50 (22.1%) workers. Irritant contact dermatitis chronica (diffuse permanent erythema with numerous telangiectasiae on the lateral portions of the face and neck, on the trunk, behind the auricles) was detected in 40 (17.7%) workers. The remaining 19 (8.4%) workers had both types of dermal change. All examined workers complained of very strong itching. The results of the patch tests confirmed the irritant activity of the ceramic fibres. Erythema without oedema, persisting for up to 96 h, appeared at the places where the fibres had been applied to the skin in 44 (19.5%) workers. In addition, the irritant activity of the fibres has been shown to be correlated with their thickness. The Thermowool fibre was the weakest irritant, because it did not contain filaments above 3 microns in diameter; the L-2 fibre containing 6.3% filaments above 3 microns caused somewhat stronger skin irritation; while the L-3 fibre, which contained 11.1% filaments thicker than 3 microns, was the strongest irritant. A few cases of allergy to nickel, chromium and colophony (rosin) were also detected.

Code(s): 8.
McDonald, J. W., F. Alvarez and C. A. Keller. (2000). "Pulmonary alveolar proteinosis in association with household exposure to fibrous insulation material." Chest. 117 (6): 1813-7.
We report the case of a 35-year-old woman who developed pulmonary alveolar proteinosis requiring multiple lavage treatments, in association with household exposure to ventilation system dust comprised at least partially by a cellulose fire-resistant fibrous insulation material. Scanning electron microscopy with energy- dispersive x-ray analysis documented the presence of spectral peaks consistent with the insulation material in transbronchial biopsy tissue. The patient showed symptomatic improvement once exposure to the insulation material had ceased. We believe that this case demonstrates an unusual association with pulmonary alveolar proteinosis. This case emphasizes the broad differential diagnosis for this histologic injury pattern and the need to thoroughly investigate environmental exposures in patients with unexplained pulmonary disease.

Code(s): 8.
Meysman, M., I. Monsieur, M. Noppen and W. Vincken. (2000). "Localised obliterative bronchitis due to non-occupational mineral dust inhalation." Acta Clin Belg. 55 (6): 341-3.

We present a 56-year-old woman with an infiltrate in the right middle lobe secondary to obstruction of the right middle lobe bronchus by extensive submucosal fibrosis. This unique stenotic lesion of a central bronchus was caused by a domestically acquired localised central obstructive bronchitis due to the inhalation of mixed dust fibers, in the absence of advanced silicosis. This complication is a rare presentation of the myriad of pulmonary diseases associated with mineral dust inhalation.

Code(s): 8.
Hansen, E., F. Rasmussen, F. Hardt and O. Kamstrup. (1999). "Lung function and respiratory health of long-term fiber-exposed stonewool factory workers." American Journal of Respiratory and Critical Care Medicine; 160 (2). 1999. 466-472.
BIOSIS COPYRIGHT: BIOL ABS. The present study was undertaken to examine the respiratory health of a Danish workforce exposed to man-made vitreous fibers (MMVF) during production. Workers with more than 5 yr occupational exposure to MMVF (n = 377) were compared to a group without MMVF exposure (n = 381). Respiratory health was assessed by questionnaire, dynamic spirometry, and measurement of transfer factor. Overall response rate was 63%. A sample of nonresponders was assessed by questionnaire and spirometry. On most spirom in the two groups. There is no indication of excess risk of lung fibrosis. However, a number of exposed workers have some degree of airflow obstruction, which cannot be explained by known confounders. An additive or synergistic action between smoking and fiber exposure on airflow obstruction can be speculated.

Code(s): 8.
Maxim, L. D., R. W. Mast, M. J. Utell, C. P. Yu, P. M. Boymel, B. K. Zoitos and J. E. Cason. (1999). "Hazard assessment and risk analysis of two new synthetic vitreous fibers." Regul Toxicol Pharmacol. 30 (1): 54-74.
Isofrax and Insulfrax are two new synthetic vitreous fibers (SVFs) developed for high-temperature insulation (1800-2300 degrees F) applications. In an attempt to significantly reduce or eliminate the potential of adverse health effects, these two fibers were specifically designed to have high solubility and, thus, low in vivo biodurability. In this paper, we review the effects of chemical composition on biodurability, in vitro fiber dissolution rates (K(dis)), and the relevance and relationship of K(dis) to pulmonary fibrosis and lung tumors in chronic rat inhalation studies. We also examine the correlations between K(dis) and weighted in vivo half-life (t(0.5)) of long fibers (>20 microm) and their relation to pulmonary effects in chronic rat inhalation bioassays. Predictions for outcomes of inhalation bioassays and development of nonsignificant risk levels of exposure are provided. Additionally, justification for the use of inhalation versus noninhalation animal data is provided as is a brief review of human health effects of SVFs. We conclude, inter alia, that Isofrax and Insulfrax have low biodurability, would not be expected to produce either pulmonary fibrosis or lung tumors in a well-designed animal inhalation bioassay, have weighted half-lives beneath the threshold established by the European Union for classification as a carcinogen, and based on epidemiological data for SVFs would not be expected to result in incremental cancer in human cohorts. Finally, it is estimated that approximately 90% of workplace exposure concentrations of these materials would be beneath 1 f/cc. At a concentration of 1 f/cc, neither fiber would be expected to result in an incremental working lifetime cancer risk greater than 10(-5).

Code(s): 8.
Riboldi, L., G. Rivolta, M. Barducci, G. Errigo and O. Picchi. (1999). "[Respiratory disease caused by MMVF fibers and yarn]." Med Lav. 90 (1): 53-66.
The non-carcinogenic effects of vitreous fibres on the human respiratory apparatus have been the subjects of numerous studies on large exposed populations. No evidence seems to have been produced of the existence of a fibrogenic effect. However, no definite and agreed opinion has yet been expressed by the main Agencies and Institutions working in the field of prevention. As a contribution to the discussion, the paper presents the experience of the Clinica del Lavoro of Milano involving 1000 subjects who underwent broncho-alveolar lavage during assessment and checking for suspected occupational respiratory disease. A group of 23 cases was selected who were exposed to vitreous fibres without other significant exposures to factors considered hazardous for the respiratory apparatus, especially asbestos. We observed 7 cases of alveolitis; 6 cases with pleural thickening; 2 cases of interstitial disease. On the basis of the nature of exposure (duration, latency from beginning and from the end of hazardous occupation), of the data obtained from the examination of the bronchial lavage liquid (presence of vitreous fibres, siderocytes, cellularity), and of the clinical and laboratory data (X-ray, PFR), the view expressed is tendentially reassuring concerning the possible effects of vitreous fibres on the respiratory apparatus. Although the existence of an irritative type of lesion that manifests in the form of alveolitis and localised pleural thickening seems possible, albeit in a limited number of cases, it does however appear much more difficult to admit the existence of a fibrogenic effect.

Code(s): 8.
Wang, Q. E., C. H. Han, W. D. Wu, H. B. Wang, S. J. Liu and N. Kohyama. (1999). "Biological effects of man-made mineral fibers (I) - Reactive oxygen species production and calcium homeostasis in alveolar macrophages." Industrial Health Jan. 1999, Vol.37, No.1, p.62-67. Illus. 23 ref.
Ten types of standard mineral fibre samples (JFM fibres) were tested for their cytotoxicity in alveolar macrophages (AM) in vitro experiments, in which UICC chrysotile B was used as a positive control. The cytotoxicity tests included the production of superoxide

anion radical and hydrogen peroxide, depletion of glutathionee (GSH) and increase of intracellular free calcium. Results showed that chrysotile and most of the ten mineral fibres could increase the production of superoxide anion and hydrogen peroxide, deplete the concentration of GSH and increase the level of free intracellular Ca²+ in AM. All the effects of JFM fibres were lower than that induced by UICC chrysotile B. Although the cytotoxicity of JFM fibres was lower than that of asbestos, these mineral fibres should be used with care in industry. Topics: animal experiments; chrysotile; potassium titanate; titanium oxide; asbestos; wollastonite; silicon carbide; calcium; hydrogen peroxide; glutathione; ceramic fibres; cytotoxic effects; glass fibre; in vitro experiments; lung; macrophages; man-made fibres; mineral fibres; mineral wool.

Code(s): 8.
Albin, M., G. Engholm, N. Hallin and L. Hagmar. (1998). "Impact of exposure to insulation wool on lung function and cough in Swedish construction workers." Occup Environ Med. 55 (10): 661-7.
OBJECTIVES: To investigate whether application of insulation wool adversely affects lung volumes and increases the occurrence of symptoms of airway irritation. METHODS: Data from nationwide health check ups in 1981-93 of male construction workers born in 1955 or later were used to investigate cross sectional (n = 96,004) and longitudinal (n = 26,298) associations between lung volumes, vital capacity (VC), and forced expiratory volume in one second (FEV1) and exposure to insulation wool by combining a job exposure matrix (JEM) and self reported exposure. Data on 12 month prevalence of persistent cough not associated with the common cold was available for the period 1989-92. Potential confounding from smoking, exposure to asbestos, silica, and isocyanates, was considered in the analyses. RESULTS: For those in the highest exposure category (self reported duration of exposure of > or = 11 years, and high exposure according to the JEM) VC was on average 2.5 cl lower (95% CI -6.5 to 1.5) than in those with no exposure. The corresponding figures for FEV1 was -2.4 cl (95% CI -6.1 to 1.3). In the longitudinal analyses, the yearly change in VC between the first and last spirometry for those in the highest exposure category was 0.50 cl (95% CI -0.97 to 1.98) less than in the unexposed category. The corresponding figure for FEV1 was 0.89 cl (95% CI - 0.70 to 2.06). High exposure to insulation wool, asbestos, or silica, during the 12 months preceding the check up was associated with increased odds ratios (ORs) for persistent cough of the same magnitude as current smoking. CONCLUSIONS: The results indicate no effects on VC or FEV1 from exposure to insulation wool. Recent exposure to insulation wool, asbestos, and silica was associated with an increased prevalence of persistent cough.

Code(s): 8.
Boffetta, P., D. Sali, H. Kolstad, D. Coggon, J. Olsen, A. Andersen, A. Spence, A. C. Pesatori, E. Lynge, R. Frentzel-Beyme, J. Chang-Claude, I. Lundberg, M. Biocca, V. Gennaro, L. Teppo, T. Partanen, E. Welp, R. Saracci and M. Kogevinas. (1998). "Mortality of short-term workers in two international cohorts." J Occup Environ Med. 40 (12): 1120-6.
The purpose of this study was to compare the pattern of mortality of blue-collar workers employed less and more than 1 year in the man-made vitreous fiber (MMVF) and the reinforced plastic industries, the latter group being exposed to styrene. We conducted an analysis among 21,784 workers with less than 1 year of employment (short-term workers) and 19,117 workers with 1 or more years of employment (long-term workers) employed in eight European countries. We conducted analyses based on external as well as internal comparisons. In both cohorts, the standardized mortality ratio for all causes among short-term workers was approximately 40% higher, compared with that for longer-term workers. In internal comparisons, the difference was reduced to 9% in the MMVF cohort and 11% in the styrene cohort. Workers with less than 1 month of employment displayed an increased mortality in both cohorts and in most countries. The increased mortality among short-term workers was not concentrated shortly after they quit employment. In both cohorts, short-term workers had a higher mortality from external causes, while little difference was seen in mortality from ischemic heart disease and malignant neoplasms. Although extra-occupational factors may contribute to increase the mortality of short-term workers and, in particular, of those employed for less than 1 month, the difference observed in analyses adjusted for characteristics of employment suggested a relatively small difference in mortality from most causes.

Code(s): 8.
Lemasters, G. K., J. E. Lockey, L. S. Levin, R. T. McKay, C. H. Rice, E. P. Horvath, D. M. Papes, J. W. Lu and D. J. Feldman. (1998). "An industry-wide pulmonary study of men and women manufacturing refractory ceramic fibers." Am J Epidemiol. 148 (9): 910-9.
An industry-wide pulmonary morbidity study was undertaken to evaluate the respiratory health of employees manufacturing refractory ceramic fibers at five US sites between 1987 and 1989. Refractory ceramic fibers are man-made vitreous fibers used for high temperature insulation. Of the 753 eligible current employees, 742 provided occupational histories and also completed the American Thoracic Society respiratory symptom questionnaire; 736 also performed pulmonary function tests. Exposure to refractory ceramic fibers was characterized by classifying workers as production or nonproduction employees and calculating the duration of time spent in production employment. The risk of working in the production of refractory ceramic fibers and having one or more respiratory symptoms was estimated by adjusted odds ratios and found to be 2.9 (95 percent confidence interval 1.4-6.2) for men and 2.4 (95 percent confidence interval 1.1-5.3) for women. The effect of exposure to refractory ceramic fibers on forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), the ratio of the two (FEV1/FVC), and forced expiratory flow (liters/second) between 25

percent and 75 percent of the FVC curve (FEF(25-75)) was evaluated by multiple regression analysis using transformed values adjusted for height, by dividing by the square of each individual's height. For men, there was a significant decline in FVC for current and past smokers of 165.4 ml ($p < 0.01$) and 155.5 ml ($p = 0.04$), respectively, per 10 years of work in the production of refractory ceramic fibers. For FEV1, the decline was significant ($p < 0.01$) only for current smokers at 134.9 ml. For women, the decline was greater and significant for FVC among nonsmokers, who showed a decrease of 350.3 ml ($p = 0.05$) per 10 years of employment in the production of refractory ceramic fibers. These findings indicate that there may be important sex differences in response to occupational and/or environmental exposure.

Code(s): 8.
Lockey, J. E., L. S. Levin, G. K. Lemasters, R. T. McKay, C. H. Rice, C. R. Hansen, D. M. Papes, S. Simpson and M. Medvedovic. (1998). "Longitudinal estimates of pulmonary function in refractory ceramic fiber manufacturing workers." American Journal of Respiratory and Critical Care Medicine; 157 (4 Part 1). 1998. 1226-1233.
BIOSIS COPYRIGHT: BIOL ABS. Refractory ceramic fibers (RCF) are man-made vitreous fibers (MMVF) used in high-temperature industrial applications. Between 1987 and 1994, a prospective study evaluated pulmonary function of 361 male workers currently employed in RCF manufacturing and related operations for plausibility of a causal relationship between RCF exposure and pulmonary function changes. Workers included in the analysis provided at least five pulmonary function tests. The exposure-response relationship was modeled with two exposure variables: years in a production job, and cumulative fiber exposure (fiber-mo/cc). Comparison groups were nonproduction workers and workers with up to 15 fiber-mo/cc cumulative exposure. A statistically significant decrease in FVC was demonstrated among workers employed in production jobs more than 7 yr prior to initial test. A similar but nonstatistically significant result was demonstrated for FVC in workers with greater than 60 fiber-mo/cc cumulative exposure pr MH - RESPIRATORY TRACT DISEASES/PHYSIOPATHOLOGY

Code(s): 8.
Velichkovskii, B. T. (1998). "Main pathogenic mechanisms of occupational pulmonary diseases caused by dust. Part I. From experiments to a concept." Meditsina Truda I Promyshlennaya Ekologiya; 0 (10). 1998. 28-38.
Biosis copyright: biol abs. rrm continuing education human pathogen occupational health pulmonary medicine toxicology pathogenetic mechanism occupational pulmonary disease pulmonary fibrosis prophylaxis therapy phagocyte active forms of oxygen generation mechanism catalytic activity energy deficiency intracellular hypoxia asbestos toxin iron oxides coal mineral carcinogenicity emphysema chronic obstructive bronchitis physical stress silica silicosis clinical features dust-induced morphological features respiratory system disease immune system activation toxicity

Code(s): 8.
Luoto, K., M. Holopainen, M. Sarataho and K. Savolainen. (1997). "Comparison of cytotoxicity of man-made vitreous fibres." Ann Occup Hyg. 41 (1): 37-50.
The purpose of the study was to compare the cytotoxicity of man-made vitreous fibres (MMVFs): four refractory ceramic fibres (RCFs 1-4), two glasswool fibres (MMVF 10 and 11), a rockwool fibre (MMVF 21) and a slagwool fibre (MMVF 22). The ability of the fibres to induce haemolysis in sheep erythrocytes, to release lactate dehydrogenase (LDH) from rat alveolar macrophages (AM) and to increase the production of reactive oxygen metabolites (ROMs) in human polymorphonuclear leukocytes (PML) was studied. To assess the relative cytotoxicity of MMVFs, their toxicity was compared with that induced by quartz, chrysotile or titanium dioxide. MMVFs induced a modest, but dose- dependent, increase of haemolysis at doses of 0.5, 2.5 and 5.0 mg ml-1. The amount of haemolysis and LDH release induced by MMVFs was generally similar to that induced by titanium dioxide. Glasswool fibre MMVF 10 induced less LDH release from rat AM than rockwool MMVF 21 or slagwool MMVF 22 fibres, whereas glasswool fibre MMVF 11 induced less LDH release than slagwool fibre MMVF 22 ($P < 0.05$). All fibres also dose- dependently increased the production of ROMs at doses between 25 and 500 micrograms ml-1. The shapes of the time-courses of MMVF-induced production of ROMs suggest that the mechanisms whereby the different fibres induce ROM production may exhibit similar features. There are clear-cut differences in the potency of various MMVFs to induce cytotoxicity and oxidative burst. The present results also emphasize the importance of using several measures of toxicity when assessing the biological activity of various fibres in vitro.

Code(s): 8.
Vu, V. T. and D. Y. Lai. (1997). "Approaches to characterizing human health risks of exposure to fibers." Environ Health Perspect. 105 Suppl 5 1329-36.
Naturally occurring and man-made (synthetic) fibers of respirable sizes are substances that have been identified by the U.S. Environmental Protection Agency (U.S. EPA) as priority substances for risk reduction and pollution prevention under the Toxic Substances Control Act (TSCA). The health concern for respirable fibers is based on the link of occupational asbestos exposure and environmental erionite fiber exposure to the development of chronic respiratory diseases, including interstitial lung fibrosis, lung cancer, and mesothelioma in humans. There is also considerable laboratory evidence indicating that a variety of fibers of varying

physical and chemical characteristics can elicit fibrogenic and carcinogenic effects in animals under certain exposure conditions. This paper discusses key scientific issues and major default assumptions and uncertainties pertaining to the risk assessment of inhaled fibers. This is followed by a description of the types of assessment performed by the U.S. EPA to support risk management actions of new fibers and existing fibers under TSCA. The scope and depth of these risk assessments, however, vary greatly depending on whether the substance under review is an existing or a new fiber, the purpose of the assessment, the availability of data, time, and resources, and the intended nature of regulatory action. In general, these risk assessments are of considerable uncertainty because health hazard and human exposure information is often incomplete for most fibers. Furthermore, how fibers cause diseases and what specific determinants are critical to fiber-induced toxicity and carcinogenicity are still not completely understood. Further research to improve our knowledge base in fiber toxicology and additional toxicity and exposure data gathering are needed to more accurately characterize the health risks of inhaled fibers.

Code(s): 8.
Thriene, B., A. Sobottka, H. Willer and J. Weidhase. (1996). "Man-made mineral fibre boards in buildings--health risks caused by quality deficiencies." Toxicol Lett. 88 (1-3): 299-303.
The Institute of Hygiene was requested to determine causes and scope of health complaints made by the employees of Haldensleben district administration after sound absorbing mineral fibre boards had been installed as suspended ceilings. The boards were coated with a lean water-carried paint; however, the edges, which were partially frayed, were not coated. The air inside the rooms was measured on all four storeys of the building, followed by scanning electron microscopy in compliance with VDI Code 3492. In addition, measurements showed fibres with diameters of > 3 microns which are not subject to the regulations for carcinogenic substances, but, in contrast to the thinner fibres, they may cause irritations of skin and mucosa. The employees were questioned about their health problems. At the beginning of 1994, a total of 79 of the 133 employees complained about itching, reddening and burning of their eyes as well as irritations of the upper respiratory tract. More than 50% had consulted a doctor. Late in 1994, another questionnaire survey was completed. The fibre content of the office air was determined to vary from 1000 to 3500 fibres/m3 and, in addition, 100-200 fibres with diameters of > 3 microns. Our investigations showed that there is an interrelationship between the degree of dust accumulation in the offices and health complaints. Independently of the current discussion of the cancer causing potential of thin man-made mineral fibres, the very long and thick mineral fibres (> 3 microns in diameter) are of topical importance to health.

Code(s): 8.
Vaughan, G. L. and S. A. Trently. (1996). "The toxicity of silicon carbide whiskers: A review." Journal of Environmental Science and Health Part a Environmental Science and Engineering & Toxic and Hazardous Substance Control; 31 (8). 1996. 2033-2054.
BIOSIS COPYRIGHT: BIOL ABS. Epidemiological studies of workers occupationally exposed to man-made mineral fibers have revealed a significant connection between exposure and the incidence of pulmonary pathologies including cancer. Although surface chemistry and related characteristics are factors in particle toxicity, most workers agree that the strongest correlate with toxicity is particle size and geometry. From the perspective of data available from exposure in animal models and in vitro experiments, one might expect silicon carbide whiskers to be at least as toxic as crocidolite asbestos. In several studies of workers involved in the production of SiC, fibers of silicon carbide were found associated with permanent respiratory dysfunction and lung cancer. Until competent studies of adequate duration in animal models are performed or epidemiological evidence is collected, a "no effect" level can not be established. Measures should be taken in the work place to prevent pulmonary exposure to silico

Code(s): 8.
Bignon, J., P. Brochard, G. Gibbs and eds. (1995). "MMF: Assessment of toxicity of man-made fibres - Papers from a workshop held in Paris, France, 3-4 February 1994." Annals of Occupational Hygiene Oct. 1995, Vol.39, No.5. p.633-781. Illus. Bibl.ref.
Main subjects dealt with in papers presented at a workshop on the assessment of toxicity of man-made fibres held in Paris on 3-4 February 1994 were: chronic inhalation studies of man-made vitreous fibres; biopersistence of man-made vitreous fibres; evaluation of the oncogenic potential of man-made vitreous fibres; inhalation toxicology studies with para-aramid fibrils; in vivo biological activity of ceramic fibres; advantages and limits of in vivo screening tests; deposition of inhaled asbestos and man-made mineral fibres in the respiratory tract.

Code(s): 8.
Hart, G. A., L. M. Kathman and T. W. Hesterberg. (1994). "In Vitro Cytotoxicity of Asbestos and Man-Made Vitreous Fibers: Roles of Fiber Length, Diameter and Composition." Carcinogenesis, Vol. 15, No. 5, pages 971-977, 29 references, 1994.
The impact of fiber parameters on in-vitro toxicity to cells and the validity of an in-vitro test system as a toxic screen for fibrous materials were investigated. Size selected inorganic test fibers that represented a range of different diameters, lengths and compositions were studied to determine their toxicity to Chinese-hamster-ovary (CHO) cells. Inhibition of proliferation, induction of micronuclei and polynuclei and viability were the toxic end points monitored. The findings indicated that the primary toxic effect of fibers on CHO cells is the induction of nuclear morphologic alterations resulting in cytostasis. The fiber diameter had little or no impact on in-vitro

toxicity when concentrations were calculated as fibers/square centimeter. Fiber length was directly proportional to in-vitro toxicity. The toxicity of asbestos (1332214) and vitreous fibers to CHO cells was not affected by composition. Recent rodent inhalation studies using the same test fibers do not coincide in their findings with the results of these studies in regard to the lack of compositional effect in CHO cells. The authors suggest that CHO cells may not be an appropriate in-vitro model of fiber pathogenesis and would not constitute a valid toxicologic screening system for fibers.

Code(s): 8.
Morgan, A. (1994). "In Vivo Evaluation of Chemical Biopersistence of Man-Made Mineral Fibers." Environmental Health Perspectives, Vol. 102, Supplement 5, pages 127-131, 24 references, 1994.
The biopersistence of man made fibers in Wistar-rats, Fischer-rats and Syrian-hamsters was investigated. Glass fibers and experimental glass fibers with specific dissolution rates were prepared in dimension ranges. Rockwool was also studied. All samples were introduced by intratracheal instillation with suspension of the fibers in physiological saline. The lungs, trachea, and external airways were excised from the animals and centrifuged and digested, with subsequent filtration of the aliquots. Results showed that the glass fibers with diameters of 1.5 microns and lengths of 5 and 10 microns were cleared mechanically from the lungs and dissolved slowly and uniformly over 18 months. Particles of the same diameter with lengths of 30 and 60 microns dissolved rapidly in an irregular manner, sometimes producing fiber fragments. For the experimental glass fibers, rapid in-vitro dissolution rates were matched with rapid in-vivo dissolution rates. With the more durable fiber, there was no significant change in number, length, or diameter over 1 year. There was no apparent change in the rockwool fibers 18 months after administration, although some of the fibers were getting thinner at the ends than the middle, where the diameter measurements were taken. Inflammation responses were studied by bronchoalveolar lavage and analysis of the recovered cells and inflammatory mediators. Recovery of binucleate macrophages suggested that the presence of the glass fibers might interfere with mitosis. Issues with the techniques of intratracheal instillation were addressed, such as the ability to introduce particles of a size beyond the respirable range, the uniformity of the distribution, and the placement of the fibers within the airway system.

Code(s): 8, 10.
Quinn, M. M., T. J. Smith, E. A. Eisen, D. H. Wegman and M. J. Ellenbecker. (2000). "Implications of different fiber measures for epidemiologic studies of man-made vitreous fibers." Am J Ind Med. 38 (2): 132-9.
BACKGROUND: Several researchers have proposed fiber size ranges representing hypotheses about the biological activity of fibers. Each of these indices has a biologically plausible rationale, yet they propose different fiber dimensions. METHODS: Four biologically based and one standard fiber analytic method index, the NIOSH 7400 method with B rules, were evaluated in air monitoring data collected in a variety of fiber glass (FG) manufacturing settings to determine their impact on an assessment of fiber exposure for an epidemiologic study of the risk of respiratory cancer among FG production workers. RESULTS: All indices varied considerably within and among the range of fiber size distributions sampled in the FG factories. CONCLUSIONS: The asymptotic relative efficiencies (R(2)) calculated among the five indices indicate a potentially important loss of power from the use of the standard method index, if one of the biologically based indices is more closely related to the disease outcome in an epidemiologic study.

Code(s): 8, 10.
Sali, D., P. Boffetta, A. Andersen, J. W. Cherrie, J. C. Claude, J. Hansen, J. H. Olsen, A. C. Pesatori, N. Plato, L. Teppo, P. Westerholm, P. Winter and R. Saracci. (1999). "Non-neoplastic mortality of European workers who produce man made vitreous fibres." Occup Environ Med. 56 (9): 612-7.
OBJECTIVE: To study mortality from non-neoplastic diseases among European workers who produce man made vitreous fibres (MMVF). METHODS: 11,373 male workers were studied, who were employed for at least 1 year in the production of rock or slag wool (RSW), glass wool (GW), and continuous filament (CF) in 13 factories from seven European countries. Workers were followed up from the beginning of production, between 1933 and 1950 to 1990-2 and contributed 256,352 person-years of observation. Standardised mortality ratios (SMRs) were calculated with national mortalities for reference; an internal exposure-response analyses based on multivariate Poisson regression models was also conducted. RESULTS: Mortality from bronchitis, emphysema, and asthma was not increased (SMR 1.03, 95% confidence interval (95% CI) 0.82 to 1.28). In RSW workers, there was no overall increase in mortality from non-malignant renal diseases (SMR 0.97, 95% CI 0.36 to 2.11), although there was the suggestion of an increase in risk with duration of employment. Mortality from ischaemic heart disease was not increased overall (SMR 1.03, 95% CI 0.96 to 1.11), but RSW and CF workers with > or = 30 years since first employment had a higher risk. RSW and CF workers showed an increased mortality from external causes, mainly motor vehicle accidents and suicide, which was higher among workers with a short duration of employment. CONCLUSIONS: Mortality from most non-neoplastic diseases does not seem to be related to employment in the MMVF industry. The results on mortality from ischaemic heart disease and non- malignant renal diseases, however, warrant further investigations.

Code(s): 8, 10.

Chang, C. H., C. M. Wang, C. K. Ho, W. B. Su and H. S. Yu. (1996). "Fiberglass dermatitis: a case report." Kaohsiung J Med Sci. 12 (8): 491-4.
Glass fibers are the most widely distributed mineral fibers because of their multiple applications, chiefly as insulation materials, and have become important in replacing asbestos fibers. Fiberglass dermatitis is one of the most common forms of occupational dermatitis resulting from mechanical irritation. Here we report a typical case. A 30-year-old male worker handled the cutting and grinding of fiberglass mats and then mixed them with resin as reinforcing materials. He complained of intense itching after the first two weeks of employment. Erythematous macules, papules and folliculitis with excoriation developed over his arms, neck, face and upper chest. There were many transparent glass fiber spicules with the diameter around 7-10 microns detected by applying the adhesive tape against the skin lesion, followed by microscopic observation. He was much improved during hospitalization with oral antihistamine and topical steroid ointment. To prevent this occupational disease, we suggest proper procedures of production, storage, transportation and cleaning in the industrial setting and proper protective clothing in personnel to minimize the release of and exposure to glass fibers.

Code(s): 8, 10, 11.
?Hesterberg, T. W. and G. A. Hart. (1994). "A comparison of human exposures to fiberglass with those used in a react rat chronic inhalation study." Regulatory Toxicology and Pharmacology; 20 (3 Part 2). 1994. S35-S46.
BIOSIS COPYRIGHT: BIOL ABS. In a recent rat inhalation study, 2 years of exposure to high concentrations of fiberglass (FG) resulted in no treatment-related fibrosis or thoracic tumors. To determine the relevancy of this study for human risk assessment, it is important to compare the rat experimental exposure levels with those of humans. Data on human exposures were taken from several studies and included FG manufacturing, installation and removal, and ambient air. FG levels in the rat aerosol were 200,000-fold higher than indoor air, > 2000-fold higher than during FG insulation manufacturing, and > 1000-fold higher than FG batt installation. The rat aerosol was 30-fold more concentrated than the highest human exposure (blowing installation of unbound FG). Rat FG lung burden also vastly exceeded that of FG workers, which was not significantly elevated above nonworker levels. The amount of fibers/mg dry lung for the rat after lifetime exposure was > 4000-fold greater than for the FG worker

Code(s): 8, 15.
Fubini, B. (1997). "Surface reactivity in the pathogenic response to particulates." Environ Health Perspect. 105 Suppl 5 1013-20.
The peculiar characteristics of dust toxicity are discussed in relation to the processes taking place at the particle-biological medium interface. Because of surface reactivity, toxicity of solids is not merely predictable from chemical composition and molecular structure, as with water soluble compounds. With particles having the same bulk composition, micromorphology (the thermal and mechanical history of dust and adsorption from the environment) determines the kind and abundance of active surface sites, thus modulating reactivity toward cells and tissues. The quantitative evaluation of doses is discussed in comparisons of dose-response relationships obtained with different materials. Responses related to the surface of the particle are better compared on a per-unit surface than per-unit weight basis. The role of micromorphology, hydrophilicity, and reactive surface cations in determining the pathogenicity of inhaled particles is described with reference to silica and asbestos toxicity. Heating crystalline silica decreases hydrophilicity, with consequent modifications in membranolytic potential, retention, and transport. Transition metal ions exposed at the surface generate free radicals in aqueous suspensions. Continuous redox cycling of iron, with consequent activation-reactivation of the surface sites releasing free radicals, could account for the long-term pathogenicity caused by the inhalation of iron-containing fibers. In various pathogenicities caused by mixed dusts, the contact between components modifies toxicity. Hard metal lung disease is caused by exposure to mixtures of metals and carbides, typically cobalt (Co) and tungsten carbide (WC), but not to single components. Toxicity stems from reactive oxygen species generation in a mechanism involving both Co metal and WC in mutual contact. A relationship between the extent of water adsorption and biopersistence is proposed for vitreous fibers. Modifications of the surface taking place in vivo are described for ferruginous bodies and for the progressive comminution of chrysotile asbestos fibers.

Code(s): 8, 15.
Meldrum, M. (1996). "Review of fibre toxicology." HSE Books, P.O. Box 1999, Sudbury, Suffolk CO10 6FS, United Kingdom, 1996. v, 72p. 133 ref.
This review focuses on those properties of fibres that influence their toxicological hazard; it does not address the question of the tendency of fibres to become airborne. Contents: property and uses of fibres (natural and man-made mineral fibres, synthetic organic fibres); human health effects from exposure to asbestos (pulmonary fibrosis, lung cancer, mesothelioma); lung deposition and clearance; animal studies in fibre toxicity; mechanisms of fibre toxicity; fibre toxicity testing strategy; relationship between fibre size and toxicity.

Code(s): 8. 15.
group, E. w. (1996). "Toxicology of Man-made organic fibres (MMOF)." TA:ECETOC Technical Report PG:67 p YR:1996 IP: VI:69.
The established relationship between inhalation of asbestos fibres of respirable size and disease has led to a belief that all similarly

sized and shaped particles of other materials are equally dangerous to human health. Organic fibres, man-made or natural, produce small numbers of respirable fibre-shaped particulates. This report briefly describes the nature of man-made organic fibres and the release of respirable fibre-shaped particulates, reviews the available data on occupational exposure, health effects and the toxicology of man-made organic fibres, compares organic and mineral fibres and indicates data gaps and areas of research which could contribute most to risk assessment. Little is known about the generation of respirable fibre-shaped particulates during production, use and disposal of man-made organic fibres but available data on industrial exposure indicate that the exposure potential is low, typically between 0.01 and 0.1 fibres/cm3 for commodity fibres and below 0.5 fibres/cm3 for p-aramids. Much is known about the health hazards of natural organic fibres, but none of this is related or has been ascribed to fibre-shaped respirable-sized particulates. Two case reports suggest a relationship between respirable particles derived from man-made organic fibres and respiratory disease but any relationship with fibre shape is uncertain in these cases. The health effects described were different from those induced by exposure to asbestos. The few epidemiological studies on health risks from occupational exposures in the man-made organic fibre industry are inadequate to exclude or to establish a human health risk from exposure to respirable fibre-shaped particulates from man-made organic fibres. Man-made organic fibres differ from natural and man-made mineral fibres in several characteristics that determine toxicity, e.g. chemical composition, surface structure, physical characteristics of respirable fibre-shaped particulates and biodegradability. The limited toxicological database indicates that the biological activity of respirable fibre-shaped particles derived from man-made organic fibres and from natural and man-made mineral materials are quantitatively and qualitatively different. Future research should focus primarily on man-made organic fibres with more than a trivial exposure potential. Toxicological test systems, currently in use for screening and/or classification of fibres, need to be re-evaluated for their relevance to man-made organic fibres before test results can be extrapolated to any hazard. A combination of tests for cytotoxicity and genotoxicity with acute inhalation, subchronic inhalation and biodegradability studies will provide useful information. Epidemiological studies are unlikely to contribute significantly to future risk assessments, because of the apparent impossibility to establish significant differences in exposure levels and/or finding non-exposed controls; exposure in industry being of the same magnitude as in the general population.

Man-made Vitreous Fibers (MMVFs), cancer (9, 10)
—health/irritant effects, metabolism, mechanisms

Code(s): 9.
Wang, Q. E., C. H. Han, Y. P. Yang, H. B. Wang, W. D. Wu, S. J. Liu and N. Kohyama. (1999). "Biological effects of man-made mineral fibers (II)--their genetic damages examined by in vitro assay." Ind Health 1999 Jul;37(3):342-7.
In order to study and compare genetic damage induced by 10 kinds of man-made mineral fibers (JFM fibers) in cells, human lung epithelial cells (A549) were exposed to JFM fibers and chrysotile for 1 h, then single-cell gel electrophoresis (SCGE) assay was used to detect DNA strand breaks, DNA-DNA interstrand crosslink and the ability of DNA to repair; The results showed that all 10 JFM fibers could induce DNA strand breaks, DNA-DNA interstrand crosslinks and inhibit the ability of DNA repair. When human embryo lung (HEL) cells were exposed to JFM fibers and chrysotile for 24 h respectively, the chromosomal aberration was analyzed and the results showed that chrysotile and most of JFM fibers at 5.0 micrograms/ml induced structural chromosomal aberration, but all of these effects were lower than that of chrysotile and were different among them, suggesting that 10 types of JFM fibers had genotoxicity with different degree in vitro, but all of them were lower than that of chrysotile.

Code(s): 9.
Consonni, D., P. Boffetta, A. Andersen, J. Chang-Claude, J. W. Cherrie, G. Ferro, R. Frentzel-Beyme, J. Hansen, J. Olsen, N. Plato, P. Westerholm and R. Saracci. (1998). "Lung cancer mortality among European rock/slag wool workers: exposure- response analysis." Cancer Causes Control. 9 (4): 411-6.
OBJECTIVES: The purpose was to analyze the relationship between semi- quantitative indices of exposure to manmade vitreous fibers and lung cancer mortality among European rock/slag wool (RSW) workers. METHODS: The study population comprised 9,603 male workers employed in RSW production in seven factories in Denmark, Norway, Sweden, and Germany, followed up for mortality as of 1990-91. Estimates of past exposure to respirable fibers were used to calculate cumulative exposure with a 15- year lag and maximum annual exposure based on employment history up to 1977. Rate ratios were estimated via multivariate Poisson regression, adjusting for country, age, calendar year, time since first employment, and employment status. RESULTS: A total of 159 lung cancer deaths were included in the analysis of which 97 among workers with more than one year of employment. We found nonstatistically significant trends in lung cancer risk according to cumulative exposure. Relative risks (RR) in the four quartiles were 1.0 (reference), 1.3 (95 percent confidence interval [CI] = 0.8-2.4), 1.2 (CI = 0.7-2.1), and 1.5 (CI = 0.7-3.0, P test for trend = 0.4). When workers with less than one year of employment were excluded, there was no increased risk; the RRs in the four quartiles were 1.0, 0.9 (CI = 0.4-2.0), 0.8 (CI = 0.3-1.9), and 1.0 (CI = 0.4-2.7). No trend was present according to maximum annual exposure. The results were not consistent among countries. CONCLUSIONS: We found a positive association between exposure to respirable fibers and lung cancer mortality. However, the lack of statistical significance, the dependence of the results on inclusion of short-term workers, the lack of consistency among countries, and the possible correlation between exposure to respirable fibers and to other agents reduce the weight of such

evidence.

Code(s): 9.
Anonymous. (1995). "Man-Made Mineral Fibers. Assessment of Carcinogenicity." Health Council of the Netherlands: Committee on the Evaluation of the Carcinogenicity of Chemical Substances. The Hague: Health Council of the Netherlands, 1995; Publication No. 1995/18, 45 pages, 3 references, 1995.
The results of the assessment of the carcinogenicity of man made mineral fibers conducted by the Committee on the Evaluation of the Carcinogenicity of Chemical Substances were presented. This committee specifically addressed concerns and answered questions expressed by the Minister of Housing, Spatial Planning and Environment. The Committee concluded that of the six currently identified categories of man made mineral fibers, only refractory ceramic fiber was carcinogenic. The Committee also concluded that only inhalable refractory ceramic fibers appeared to present a carcinogenic risk. In response to a question on the comparative carcinogenicity of asbestos and man made mineral fibers, the Committee stated that such a comparison was not possible because of differences in the physical and chemical characteristics of these fibers. Fiber size was described as the characteristic contributing most to the degree of hazard presented by fibers.

Code(s): 9.
Konetzke, G. W. (1995). "The carcinogenicity of man-made mineral fibres." Atemwegs- Und Lungenkrankheiten; 21 (4). 1995. 194-198.
BIOSIS COPYRIGHT: BIOL ABS. This paper presents the current evidence concerning the problem of carcinogenicity of Man-made mineral fibres (MMMF), reflecting recent results in re search, experts' discussions and official statements. Experimental data clearly proved carcinogenicity of MMMF in rats using both - inhalation tests and serosa tests. But its extent depended from the different fibre types and the experimental system which had been used. In contrast epidemiological studies demonstrated no clear overall excess mortality or excess morbidity for lung cancer up to now, but there were some trends as regard to the time since first employment and early technological phases of MMMF production. The effects of ceramic fibres for humans are completely unknown yet. The conclusion from all results is that MMMF should be classified as possible carcinogenic to humans. The carcinogenic potency may be more less as compared with asbestos due to lower biopersistence and a smaller amount of respirable dust und

Code(s): 9.
Linnainmaa, K. and K. Pelin. (1995). "Carcinogenic Mode of Action of Asbestos and Man-Made Mineral Fibers in Human Mesothelial Cells." Sixth US-Finnish Joint Symposium on Occupational Health and Safety, People and Work. Research Reports 3, Proceedings of the Sixth FIOH-NIOSH Joint Symposium on Occupational Health and Safety, 8-10 August 1995, Espoo, Finland, -=H. Nordman, J. St, 1995.
Studies concerning both mesothelioma cell lines, and experimental in-vitro investigations on asbestos (1332214) and man made mineral fibers were summarized. Seven immortal cell lines from tumor samples or pleural effusions from mesothelioma patients with a history of asbestos (1332214) exposure were used. Indices such as chromosomal aberrations, gap junctional intercellular communication (GJIC), reactive oxygen species, and individual susceptibility were considered. The study results suggested that the karyotypic abnormalities and reduced GJIC, typical of tumor cells, were results of later events in the carcinogenic process of malignant mesothelioma, rather than initiating events. The effective induction of binucleate cells, and consequently, possible disruption of cell to cell adhesion and cytoskeleton leading to decreased GJIC or aneuploid cells, may be a more important early step in the fiber carcinogenesis. The current findings supported earlier data which suggested that the inflammatory cell derived free radicals and cytokines were of importance in the development of asbestos induced mesothelial cell injury. The man made mineral fibers, glass wool and rock wool, were less toxic to mesothelial cells in-vitro than the various asbestos fibers, reflecting differences in the size distribution of these fibers in the basic materials. When fibers were sized and numbered equally in the in-vitro experiments, equal results were obtained in the short term studies. The authors suggest that individual susceptibility may also be an important factor in the development of asbestos associated malignant mesothelioma.

Code(s): 9, 10.
Pohlabeln, H., K. H. J÷ckel, I. Br°ske-Hohlfeld, M. M÷hner, W. Ahrens, U. Bolm-Audorff, R. Arhelger, W. R÷mer, L. Kreienbrock, M. Kreuzer, I. Jahn and H. E. Wichmann. (2000). "Lung cancer and exposure to man-made vitreous fibers: Results from a pooled case-control study in Germany." American Journal of Industrial Medicine May 2000, Vol.37, No.5, p.469-477. 38 ref.
To investigate the association between lung cancer and occupational exposure to man-made vitreous fibres (MMVF), 3498 male patients with histologically- or cytologically-verified primary lung cancer were compared with 3541 male controls drawn at random from the general population and matched to cases by age and place of residence. A total of 304 cases and 170 controls reported to have worked with glass wool insulation or mineral wool mats. Coded as ever/never exposed, the odds ratio was 1.48 adjusted for smoking and asbestos. To exclude any confounding effect of asbestos, a group of cases and controls who insulated with glass wool or mineral wool mats only and never reported any asbestos exposure was identified, for which an odds ratio of 1.56 after adjustment for smoking

was found. This study provides some indication for an excess risk of MMVF which persists after adjustment for smoking and asbestos.

Code(s): 9, 10.
Boffetta, P., A. Andersen, J. Hansen, J. H. Olsen, N. Plato, L. Teppo, P. Westerholm and R. Saracci. (1999). "Cancer incidence among European man-made vitreous fiber production workers." Scand J Work Environ Health. 25 (3): 222-6.
OBJECTIVES: This study analyzed cancer incidence among man-made vitreous fiber workers. METHODS: A cancer incidence follow-up was conducted among 3685 rock-slag wool (RSW) and 2611 glass wool (GW) production workers employed for > or =1 year in Denmark, Finland, Norway, or Sweden, and the standardized incidence ratios (SIR) were calculated on the basis of national incidence rates. RESULTS: Overall cancer incidence was close to expectation. Lung cancer incidence was increased among the RSW [SIR 1.08, 95% confidence interval (95% CI) 0.85-1.36] and GW (SIR 1.28, 95% CI 0.91-1.74) workers. For both subcohorts, a trend was suggested for time since first employment (P- value for linear trend 0.1 and 0.2, respectively). Neither subcohort showed an association with employment during the early technological phase, when fiber exposure was high. The incidence of oral, pharyngeal, and laryngeal cancer was increased among the RSW (SIR 1.46, 95% CI 0.99- 2.07) and the GW (SIR 1.41, 95% CI 0.80-2.28) subcohorts. Despite a trend in risk for these neoplasms among the GW workers with time since first employment, the lack of a positive relation with other indirect indicators of fiber exposure points against a causal interpretation. No association between RSW or GW exposure and the risk of other neoplasms was suggested. CONCLUSIONS: These lung cancer results are similar to those of a mortality study that included a larger number of factories. For other cancers there was no suggestion of an association with RSW or GW exposure.

Code(s): 9, 10.
Consonni, D., I. Bernucci and P. A. Bertazzi. (1999). "[IARC multicenter study on neoplastic disease caused by man-made vitreous mineral fibers (MMVF)]." Med Lav. 90 (1): 67-83.
Man-made vitreous fibres (MMVF) showed carcinogenic potential in experimental animals. Epidemiological data suggested an increased mortality from lung cancer among production workers, but the interpretation is still a matter of controversy. A European study encompassing 13 plants in 7 countries pointed towards a moderate excess of lung cancer among workers employed longer than 1 year in the production of rock/slag wool (SMR = 1.34, 95% CI = 1.08-1.63) and glass wool (SMR = 1.27, 95% CI = 1.07-1.50); the latter increase was not confirmed after applying local rates to calculate expected deaths. The elevated risk among rock/slag wool producers was present even in comparison with local rates, and was associated with increasing time from first exposure, and duration of exposure. Glass wool results exhibited a less definite pattern. Smoking was excluded, although indirectly, as a sufficient alternative explanation of the increased lung cancer risk. In a few plants, exposure to asbestos had occurred in limited periods for some workers, and might have contributed to the findings. Case-control studies are under way to thoroughly investigate the relative and possibly combined role of the different exposures, either occupational or not. Cohort studies in the USA produced results closely consistent with those of the European study.

Code(s): 9, 10.
Boffetta, P. (1997). "Mortality of man-made vitreous fibre workers in Europe (Meeting abstract)." Proc Annu Meet Am Assoc Cancer Res; 38:A2003 1997.
This study was aimed to investigate mortality, in particular from lung cancer, among workers employed in production of man-made vitreous fibers, that are important substitutes of asbestos. A historical cohort study was conducted in 13 factories in seven European countries, comprising 13,788 production workers with more than one year of employment and 317,196 person-years. During 1950-1990, 4521 deaths were observed. The analysis was based on indirect standardization and Poisson regression models. These workers had a standardized mortality ratio of 1.05 (95% confidence interval 1.02-1.09), and a significant increase in mortality from lung cancer and accidents. The standardized mortality ratio for lung cancer was 1.34 (95% confidence interval 1.08-1.63, 97 deaths) among rock/slag wool workers and 1.27 (1.07-1.50, 140 deaths) among glass wool workers. In the latter group, no increase was present when local mortality rates were used. Among rock/slag wool workers, the risk of lung cancer was elevated in five out of seven factories and increased, although not significantly, with time since first employment and duration of employment. The association with estimated fiber exposure was not convincing. Mortality from other causes of deaths was not increased. Five deaths from pleural mesothelioma were reported. These results are not sufficient to conclude that the increased lung cancer risk is related specifically to exposure to rock/slag wool. However, rock/slag wool may have contributed to the increased risk.

Code(s): 9, 10.
Boffetta, P., R. Saracci, A. Andersen, P. A. Bertazzi, J. Chang-Claude, J. Cherrie, G. Ferro, R. Frentzel-Beyme, J. Hansen, J. Olsen, N. Plato, L. Teppo, P. Westerholm, P. D. Winter and C. Zocchetti. (1997). "Cancer mortality among man-made vitreous fiber production workers." Epidemiology. 8 (3): 259-68.
We have updated the follow-up of cancer mortality for a cohort study of man-made vitreous fiber production workers from Denmark, Finland, Norway, Sweden, United Kingdom, Germany, and Italy, from 1982 to 1990. In the mortality analysis, 22,002 production

workers contributed 489,551 person-years, during which there were 4,521 deaths. Workers with less than 1 year of employment had an increased mortality [standardized mortality ratio (SMR) = 1.45; 95% confidence interval (CI) = 1.37-1.53]. Workers with 1 year or more of employment, contributing 65% of person-years, had an SMR of 1.05 (95% CI = 1.02- 1.09). The SMR for lung cancer was 1.34 (95% CI = 1.08-1.63, 97 deaths) among rock/slag wool workers and 1.27 (95% CI = 1.07-1.50, 140 deaths) among glass wool workers. In the latter group, no increase was present when local mortality rates were used. Among rock/slag wool workers, the risk of lung cancer increased with time-since-first-employment and duration of employment. The trend in lung cancer mortality according to technologic phase at first employment was less marked than in the previous follow-up. We obtained similar results from a Poisson regression analysis limited to rock/slag wool workers. Five deaths from pleural mesothelioma were reported, which may not represent an excess. There was no apparent excess for other categories of neoplasm. Tobacco smoking and other factors linked to social class, as well as exposures in other industries, appear unlikely to explain the whole increase in lung cancer mortality among rock/slag wool workers. Limited data on other agents do not indicate an important role of asbestos, slag, or bitumen. These results are not sufficient to conclude that the increased lung cancer risk is the result of exposure to rock/slag wool; however, insofar as respirable fibers were an important component of the ambient pollution of the working environment, they may have contributed to the increased risk.

Code(s): 9, 10.
Lee, I. M., C. H. Hennekens, D. Trichopoulos and J. E. Buring. (1995). "Man-made vitreous fibers and risk of respiratory system cancer: a review of the epidemiologic evidence." J Occup Environ Med. 37 (6): 725-38.
Because asbestos has been demonstrated to cause lung cancer, the issue regarding safety of other fibers, including man-made vitreous fibers (MMVF), has been raised. We reviewed the available evidence, in particular the epidemiologic data, on MMVF and the risk of respiratory system cancer. Glass fibers (especially glass wool) have been studied most extensively. Taken together, the data indicate that among those occupationally exposed, glass fibers do not appear to increase risk of respiratory system cancer. Of six studies that specifically examined rock and slag wool workers, three reported excesses in respiratory system cancer among such workers. Two of these three studies, however, did not control for cigarette smoking, a powerful predictor of such cancers. There are no published studies, in humans, of refractory ceramic fibers. Future studies evaluating the potential of MMVF to increase risk of respiratory system cancer will not add to existing knowledge if investigators do not address potential confounding by cigarette smoking and other workplace carcinogens.

Code(s): 9, 10.
Lutz, W. and B. Krajewska. (1995). "An oxidative stress as a basic mechanism of carcinogenic effect of man made mineral fibres on the human body." Medycyna Pracy; 46 (3). 1995. 275-284.
BIOSIS COPYRIGHT: BIOL ABS. Man made mineral fibres have been recently introduced into industry as asbestos exchangers due to their much less harmful effect on workers' health. However, in 1988 (ARC classified such mineral Fibres as glass wool, rock wool and slag wool as probably carcinogenic for a man. The mechanism how MMMF may induce the carcinogenic process remains still unclear. It is assumed that the involvement of these fibres in the production of free oxygenic radicals is one of the most important factors contributing to the initiation of this process by MMMF. In the condition where free oxygenic radicals are produced very fast, the cell is exposed to an oxidative stress. The DNA damage is an important consequence of the oxidative stress. New oxygenic radicals may modify DNA and lead to mutation and finally they may contribute to the occurrence of neoplastic cells. OH is an oxygenic radical which most often damages DNA. It was also indicated that MMMF contributes to the increase of the num

Code(s): 9, 10.
Pelin, K., P. Kivipensas and K. Linnainmaa. (1995). "Effects of asbestos and man-made vitreous fibers on cell division in cultured human mesothelial cells in comparison to rodent cells." Environ Mol Mutagen. 25 (2): 118-25.
We report the effects of chrysotile and crocidolite asbestos, and glass and rock wool fibers (man-made vitreous fibers, MMVF) on the induction of binucleate cells in vitro. The response of human mesothelial cells (target cells in fiber carcinogenesis) and rodent cells was compared. Human primary mesothelial cells, MeT-5A cells (an immortalized human mesothelial cell line), and rat liver epithelial (RLE) cells were exposed to asbestos and MMVF samples of similar size range. Milled glass wool, milled rock wool, and titanium dioxide were used as non- fibrous particle controls. All four fiber types caused statistically significant increases in the amount of binucleate cells in human primary mesothelial cells and MeT-5A cells (in the dose range 0.5-5.0 micrograms/cm2). Chrysotile and crocidolite asbestos were more effective (1.3-3.0-fold increases) than thin glass wool and thin rock wool fibers (1.3-2.2-fold increases). However, when the fiber doses were expressed as the number of fibers per culture area, the asbestos and MMVF appeared equally effective in human mesothelial cells. In RLE cells, chrysotile was the most potent inducer of binucleation (2.9-5.0- fold increases), but the response of the RLE cells to crocidolite, thin glass wool, and thin rock wool fibers was similar to the response of the human mesothelial cells. No statistically significant increases in the number of bi- or multinucleate cells were observed in human primary mesothelial cells or RLE cells exposed to the non-fibrous dusts. In MeT- 5A cells exposed to 5 micrograms/cm2 of milled glass wool and milled rock wool, as well as in cultures exposed to 2 and 5 micrograms/cm2 of TiO2, significant increases were, however, observed. Our results show that rodent cells respond differently to mineral fibers than human cells. The results also add evidence to the

suggested importance of disturbed cell division in fiber carcinogenesis.

Code(s): 9, 11.
Plato, N., P. Gustavsson and S. Krantz. (1997). "Assessment of past exposure to man-made vitreous fibers in the Swedish prefabricated house industry." Am J Ind Med. 32 (4): 349-54.
Large quantities of man-made vitreous fibers (MMVF) are handled in the Swedish prefabricated wooden house industry. The present study is part of a program to investigate mortality, cancer incidence, and current as well as previous exposure to MMVF among workers in the Swedish prefabricated wooden house industry. Since measurements of historical fiber exposure levels are lacking, these were calculated by the application of a matrix of multipliers to recently measured MMVF levels. The multipliers represented changes over time in production rate, technical properties of the fibers, manual handling vs. automation, and ventilation control. The multipliers were based on a similar matrix, developed for the MMVF-manufacturing industry, which was modified to reflect the conditions in the wooden house industry. The model was developed for the highest-exposed job title in the study, insulators. One hundred and twenty samples of airborne fiber were taken in 11 plants to reflect current exposure levels. The highest mean fiber exposure level for insulators was assessed as 0.18 f/ml (geometric mean), which occurred during the mid-1970s, compared to 0.10 f/ml at the end of the 1980s and the early 1960s. Changes in production rate, improved ventilation control, and the surface area of the total amount of MMVF sheets handled per insulator were the most important variables of the model. No increased risk of lung cancer was found in the present industry.

Code(s): 9, 15.
Carpenter, R. L. and C. L. Wilson. (1999). "Inhalation Toxicity of Glass Fibers -A Review of the Scientific Literature." Govt Reports Announcements & Index (GRA&I), Issue 12, 2001.
Studies of workers occupationally exposed to asbestos revealed increasing incidence of mesothelioma, a rare form of lung cancer, whose underlying cause became clear in the 1965-1975 time frame (Selikoff et al., 1972; Selikoff et al., 1964; Selikoff et al., 1979), creating concern as to the causes of this disease and as to the properties of asbestos leading to this disease. Asbestos exposure can cause other forms of lung intervening 30 years. The purpose of this document is to provide the reader with needed background, summarize those investigations relevant to chaff health effect concerns and provide some insight as to the relevance of those concerns. Fibers differ from more spherical dust particles in their aerodynamic properties. For most dust particles, the particle's diameter and mass govern their persistence in the atmosphere.

Code(s): 9, 15.
Dutch Expert Committee on Occupational, S. (1995). "Man-made mineral fibers. Assessment of carcinogenicity." TA:Health Council of the Netherlands (Gezondheidsraad) PG:37 p YR:1995 IP: VI:1995/18.
Carcinogenic properties. Does the Health Council consider that all man-made mineral fibers (MMMFs) are carcinogenic, and that there is no threshold beneath which they have no effect? The Committee endorses the conclusion drawn by the Health Council DECOS (GR95)' that there is presently only evidence that one of the six currently identified categories of man-made mineral fibre (continuous filaments, glass wool, rock wool, slag wool, special purpose fibre and refractory ceramic fibre), is carcinogenic, namely refractory ceramic fibre. This conclusion is based on research into the effect on people and on animals of prolonged exposure to man-made mineral fibres by inhalation. Thus, the Committee's assessment is valid for those fibres which can be inhaled, i.e. those with a diameter of less than 3 um, a length of between 5 and 200 um and a length/diameter quotient of at least 3. The Committee does not have sufficient data at its disposal to determine the mechanism by which ceramic fibres can induce cancer; no conclusion can therefore be drawn regarding the existence of a carcinogenic threshold. Differences between fibre types. a Are there, in the Council's view, any differences between the various types of MMMF in terms of their carcinogenicity or in terms of the risks associated with exposure to such fibres? Having concluded that only refractory ceramic fibres are carcinogenic, the Committee believes that this question is no longer relevant. b If the Council considers that the risks associated with exposure to the various types of MMMF do differ, can the Council indicate how significant the differences are? See answer to question 2a. Comparison with asbestos. Does the Health Council consider that MMMFs are comparable with chrysotile asbestos fibres longer than 5 um and less than 3 um in diameter, in terms of their carcinogenicity or in terms of the risks associated with exposure? The Committee believes that man-made mineral fibres cannot be compared to asbestos because of considerable differences in their physical and chemical properties (Dav95, Mus94). The physical and chemical properties determine the hazardousness of fibres. Dimensions and residence times within the body are of particular importance in this context, and man-made mineral fibres and asbestos fibres differ significantly on both counts. Man-made mineral fibres remain within the body for considerably shorter periods than asbestos fibres; man-made mineral fibres have been detected in the lungs between a few weeks and a year or two after inhalation (depending on the type of fibre), whereas asbestos fibres have been found more than 20 years after inhalation in some cases. Man-made mineral fibres also differ from asbestos fibres in their dimensions. The finest asbestos fibres have a diameter between ten and a hundred times less than the finest man-made mineral fibres. Broadly speaking, the hazardousness of a fibre is inversely proportional to its diameter. Fibre lengths and carcinogenic properties. Is the Council able to distinguish between MMMFs of different lengths in terms of their carcinogenicity, as it distinguishes between asbestos fibres shorter

than 5 pm and those longer than 5 pm? It is the Committee's view that this question is only really relevant in relation to refractory ceramic fibres, since it does not believe the other types of man-made mineral fibre which it has considered, to be carcinogenic. The conclusions drawn by the Committee regarding refractory ceramic fibres are applicable only to those fibres which can be inhaled (see answer to question 1). The fraction which cannot be inhaled, is, by definition, not carcinogenic. Simultaneous exposure to fibres of different types. Does the Health Council consider that simultaneous exposure to fibres of different types leads to an accumulation of risk? There cannot be an accumulation of risk because only one of the types of man-made mineral fibre examined has carcinogenic properties.

Code(s): 9, 10.
Wilson, R., A. M. Langer and R. P. Nolan. (1999). "A risk assessment for exposure to glass wool." Regul Toxicol Pharmacol. 30 (2 Pt 1): 96-109.
Synthetic vitreous fibers (SVFs) have been widely used as insulation material in places where asbestos was used many years ago and therefore the hazards have been compared. Since the three principal types of asbestos fibers types have caused lung cancer at high exposures, there is a widely held belief that all fibers are carcinogenic if inhaled in large enough doses. Hence, on a morphological basis, SVFs have been studied for their carcinogenic potential. However, there is considerable evidence that differences exist among fibers in their potency to produce a carcinogenic response. In this attempt to carry out a numerical risk assessment for the installers of blown glass wool (fiber) insulation, we start with a characterization of the material; then we review the exposures both in manufacturing and installation. Neither the epidemiological studies of human exposure nor the animal studies have shown a marked hazardous effect from glass wool and we can therefore be sure that any effect that might exist is small. But in this case, as in many other situations where there is a potential hazard, society desires further reassurance and therefore we have made a mechanistic calculation. There are good estimates of the risk associated with exposure to chrysotile asbestos at high exposures and doses. We have therefore taken these numbers and discussed how much less risky an exposure to glass wool fibers might be. We conclude that for a given fiber count, glass wool is five to ten times less risky (and of course the risk might be zero). The risk for a nonsmoking installer of glass wool fiber insulation who wears a respirator is about 6 in a million (and might be zero) per year. This means that out of a million installers there might be six lung cancers from this cause every year or out of 10,000 installers there might be one in 16 years. The low risk of 6 in a million per year of a worker blowing glass wool is consistent with the fact that no one has found any of cancer attributable to the manufacture or installation of glass wool fibers in spite of diligent searches. This is compared with several other occupational risks. Nonetheless common prudence suggests that any installer of blown glass wool fiber insulation wear a respirator.

Man-made Vitreous Fibers, non-cancer and cancer (8, 9, 10)
—health/irritant effects, metabolism, mechanisms

Code(s): 8, 9.
Chiappino, G. (1999). "[Man-made vitreous fibers: current state of knowledge]." Med Lav. 90 (1): 5-9.
Artificial vitreous fibres have been used as thermal insulation since the 1930's. Experimental studies on possible pathogenic, fibrogenic or carcinogenic effects did not produce any clear results until the 1970's, when Stanton demonstrated the carcinogenic effect of these and numerous other fibrous materials after direct inoculation in the pleural cavity. In subsequent years epidemiological and experimental studies multiplied: the epidemiological investigations did not show any evident pathogenic effects on very large cohorts of workers, and experimentally the carcinogenic effect was confirmed only by inoculation of high doses of fibres, while negative results were reported in inhalatory experiments. In view of the considerably long time that has elapsed since these materials were first used, the low biopersistence of the fibres and the now consolidated results of a large amount of reliable research, it is today possible to affirm that artificial vitreous fibres are not a hazard for the workers who produce and use them. Since current production in Europe involves mostly large diameter, non respirable fibres or fibres with extremely low biopersistence, in accordance with precise European Union recommendations, we may look to the future without undue concern.

Code(s): 8, 9.
Harrison, P. T., L. S. Levy, G. Patrick, G. H. Pigott and L. L. Smith. (1999). "Comparative hazards of chrysotile asbestos and its substitutes: A European perspective." Environ Health Perspect. 107 (8): 607-11.
Although the use of amphibole asbestos (crocidolite and amosite) has been banned in most European countries because of its known effects on the lung and pleura, chrysotile asbestos remains in use in a number of widely used products, notably asbestos cement and friction linings in vehicle brakes and clutches. A ban on chrysotile throughout the European Union for these remaining applications is currently under consideration, but this requires confidence in the safety of substitute materials. The main substitutes for the residual uses of chrysotile are p-aramid, polyvinyl alcohol (PVA), and cellulose fibers, and it is these materials that are evaluated here. Because it critically affects both exposure concentrations and deposition in the lung, diameter is a key determinant of the intrinsic hazard of a fiber; the propensity of a material to release fibers into the air is also important. It is generally accepted that to be pathogenic to the lung or pleura, fibers must be long, thin, and durable; fiber chemistry may also be significant. These basic principles are used in a

pragmatic way to form a judgement on the relative safety of the substitute materials, taking into account what is known about their hazardous properties and also the potential for uncontrolled exposures during a lifetime of use (including disposal). We conclude that chrysotile asbestos is intrinsically more hazardous than p-aramid, PVA, or cellulose fibers and that its continued use in asbestos-cement products and friction materials is not justifiable in the face of available technically adequate substitutes.

Code(s): 8, 9.
De Vuyst, P., P. Dumortier, G. M. H. Swaen, J. C. Pairon and P. Brochard. (1995). "Respiratory Health Effects of Man-Made Vitreous (Mineral) Fibres." European Respiratory Journal, Vol. 8, No. 12, pages 2149-2173, 169 references, 1995.
This review covered the current knowledge of the respiratory effects of exposure to man made vitreous fibers (MMVF). The definition and classification of MMVF were discussed, particularly considering terminology, production, chemical composition, uses, thermal behavior, additives and contaminants, size characteristics, historical background, biopersistence, biometriology, industrial and environmental hygiene data, and airborne concentrations. The results of in-vitro studies were reviewed, including findings of cytotoxicity, genotoxicity, inflammatory and fibrinogenic processes. The findings of inhalation studies and intracavity studies were also reviewed. Human data were presented concerning nonmalignant respiratory diseases such as lung fibrosis, pleural lesions, chronic obstructive pulmonary disease, emphysema, chronic bronchitis, and asthma. Evidence concerning the risk of malignant respiratory diseases, including lung cancer and mesothelioma, was also presented.

Code(s): 8, 9.
Glass, L. R., R. C. Brown and J. A. Hoskins. (1995). "Health effects of refractory ceramic fibres: scientific issues and policy considerations." Occup Environ Med. 52 (7): 433-40.
OBJECTIVES--To review the scientific literature on the health effects of refractory ceramic fibres (RCFs). The adverse effects of exposure to asbestos has led to concern about the potential for other fibrous materials to cause diseases. For this reason the human populations most heavily exposed to synthetic mineral fibres have been examined for any adverse effects and many types of fibre have been studied in animal experiments. One type of man made vitreous fibres (MMVFs), refractory ceramic fibres (RCFs), are principally used in thermal insulation at high temperatures--up to 1400 degrees C. As manufactured RCFs exist in a glassy, non-crystalline (sometimes called amorphous) state, they have various compositions, physical properties, and sized fibres. METHODS-- All reports on the health effects of RCFs available up to the end of 1994 have been examined and the scientific literature reviewed although all publications have not necessarily been referenced. CONCLUSIONS--In recent inhalation experiments conducted with both rats and hamsters at the Research and Consulting Company, Geneva, at the highest dose tested (30 mg/m3) there was an increased incidence of tumours in both species. Lower doses were only examined in the rat and at these doses there was no significant excess of lung tumours. Epidemiological investigations of workers engaged in the manufacture of ceramic fibres have shown a small excess of pleural plaques. This phenomenon is being further investigated but could be due to confounding exposures. The populations available for study are small and their exposures fairly short, but it is considered prudent that they should remain under surveillance for some time to come. This is despite the fact that present exposures in the ceramic fibre industry are low (< 1 f/ml) and are being reduced.

Code(s): 8, 9, 10.
Morton, W. E. (2002). "Historical cohort study of US man-made vitreous fiber production workers." J Occup Environ Med. 44 (2): 106-8.

Code(s): 8, 9, 10.
Marsh, G. M., J. M. Buchanich and A. O. Youk. (2001). "Historical cohort study of US man-made vitreous fiber production workers: VI. Respiratory system cancer standardized mortality ratios adjusted for the confounding effect of cigarette smoking." J Occup Environ Med. 43 (9): 803-8.
To date, the US cohort study of man-made vitreous fiber workers has provided no consistent evidence of a relationship between man-made vitreous fiber exposure and mortality from malignant or non-malignant respiratory disease. Nevertheless, there have been small, overall excesses in respiratory system cancer (RSC) among workers from the fiberglass and rock/slag wool production plants included in the study that were unexplained by estimated worker exposures to respirable fiber or other agents present in the plants. The present investigation was designed to provide a quantitative estimate of the extent to which the overall excess in RSC mortality observed at the total cohort level among male fiberglass and rock/slag wool workers is a result of the positive confounding effects of cigarette smoking. Because cigarette- smoking data were neither available nor obtainable at the individual level for all members of the fiberglass and rock/slag wool cohorts, we used the "indirect" method to adjust RSC standardized mortality ratios (SMRs) at the group (cohort and plant) level. Our adjustment suggested that cigarette smoking accounts for all of the 7% and 24% excesses in RSC observed, respectively, for the male fiberglass and rock/slag wool cohorts in the latest mortality updates. The same conclusion was reached regardless of which of several alternative formulations were used to adjust local rate-based RSC SMRs. We found that our smoking adjustments were robust with respect to several alternative characterizations and (with the exception of one fiberglass plant) produced adjusted RSC SMRs that were lower than their unadjusted counterparts. Further, all statistically significantly elevated

unadjusted SMRs were reduced to not statistically significant levels. These results reaffirm that RSC SMRs based on US and local rates must take into account the potential confounding effects of cigarette smoking. They also suggest that the use of local county mortality rate- based SMRs may not help to adjust for cigarette smoking to the degree suggested by some investigators.

Code(s): 8, 9, 10.
Marsh, G. M., A. O. Youk, R. A. Stone, J. M. Buchanich, M. J. Gula, T. J. Smith and M. M. Quinn. (2001). "Historical cohort study of US man-made vitreous fiber production workers: I. 1992 fiberglass cohort follow-up: initial findings." J Occup Environ Med. 43 (9): 741-56.
This 1986 to 1992 update and expansion of an earlier historical cohort study examined the 1946 to 1992 mortality experience of 32,110 workers employed for 1 year or more during 1945 to 1978 at any of 10 US fiberglass (FG) manufacturing plants. Included are (1) a new historical exposure reconstruction for respirable glass fibers and several co- exposures (arsenic, asbestos, asphalt, epoxy, formaldehyde, polycyclic aromatic hydrocarbons, phenolics, silica, styrene, and urea); and (2) a nested, matched case-control study of 631 respiratory system cancer (RSC) deaths in male workers during 1970 to 1992 with interview data on tobacco smoking history. Our findings to date from external comparisons based on standardized mortality ratios (SMRs) in the cohort study provide no evidence of excess mortality risk from all causes combined, all cancers combined, and non-malignant respiratory disease. Also, excluding RSC, we observed no evidence of excess mortality risk from any of the other cause-of-death categories considered. For RSC among the total cohort, we observed a 6% excess (P = 0.05) based on 874 deaths. Among long-term workers (5 or more years of employment) we observed a not statistically significant 3% excess based on 496 deaths. Among the total cohort, we observed increases in RSC SMRs with calendar time and time since first employment, but these were less pronounced among long-term workers. RSC SMRs were not related to duration of employment among the total cohort or long-term workers. In an externally controlled analysis of male workers at risk between 1970 and 1992, we observed no association between RSC SMRs and increasing exposure to respirable FG. Our findings to date from internal comparisons based on rate ratios in the case-control study of RSC were limited to analyses of categorized study variables with and without adjustment for smoking. On the basis of these analyses, the duration of exposure and cumulative exposure to respirable FG at the levels encountered at the study plants did not appear to be associated with an increased risk of RSC. RSC risk also did not seem to increase with time since first employment. There is some evidence of elevated RSC risk associated with non-baseline levels of average intensity of exposure to respirable glass, but when adjusted for smoking this was not statistically significant, and there was no apparent trend with increasing exposure. This same pattern of findings was observed for duration of exposure, cumulative exposure, and average intensity of exposure to formaldehyde. None of the other individual co-exposures encountered in the study plants appeared to be associated with an increased risk of RSC. The primary focus of ongoing analyses is to determine the extent to which our present findings are robust to alternative characterizations of exposure.

Code(s): 8, 9, 10.
Stone, R. A., A. O. Youk, G. M. Marsh, J. M. Buchanich, M. B. McHenry and T. J. Smith. (2001). "Historical cohort study of US man-made vitreous fiber production workers: IV. Quantitative exposure-response analysis of the nested case- control study of respiratory system cancer." J Occup Environ Med. 43 (9): 779-92.
As part of the 1992 update of an historical cohort study of 32,110 workers employed for at least 1 year in any of 10 US fiberglass manufacturing plants, a nested case-control study was done in which data on tobacco smoking were obtained for 631 male case subjects with respiratory system cancer (RSC) and 570 control subjects matched on age and year of birth. In this more extensive analysis of the nested case- control data, we provide a detailed assessment of the most prominent findings from the initial report. We expand the scope of the analysis to consider quantitative measures of exposure to respirable fibers (RFib), formaldehyde (FOR), and silica (Sil) and consider these and other exposures together in the same model. We investigate the functional form of possible exposure-response relationships between RSC risk, RFib, and FOR. In addition, we address the statistical issues of collinearity, effect modification, and potential confounding by coexposures. All analyses are adjusted for smoking. Neither measure of exposure to RFib (average intensity of exposure or cumulative exposure) was statistically significantly associated with RSC risk in any of the hundreds of fractional polynomial models considered. This more extensive analysis has substantiated our initial finding of no apparent exposure-response relationship between RSC risk and either cumulative or average intensity of exposure to RFib at the levels experienced by these workers. This study provides some evidence of increased RSC risk among workers at the higher observed levels of average intensity of exposure to FOR and/or Sil. No positive associations were identified between RSC risk and any of the other exposures considered in this case- control study.

Code(s): 8, 9, 10.
Youk, A. O., G. M. Marsh, R. A. Stone, J. M. Buchanich and T. J. Smith. (2001). "Historical cohort study of US man-made vitreous fiber production workers: III. Analysis of exposure-weighted measures of respirable fibers and formaldehyde in the nested case-control study of respiratory system cancer." J Occup Environ Med. 43 (9): 767-78.
The most recent findings of our nested case-control study of respiratory system cancer (RSC) among male fiberglass workers showed some evidence of elevated RSC risk associated with non-baseline levels of average intensity of exposure (AIE) to respirable fibers

(RFib). When adjusted for smoking, this was not statistically significant, and no trend was apparent with increasing levels of exposure. Similar findings for RSC were noted for both cumulative exposure (Cum) and AIE to formaldehyde (FOR). In this reanalysis of our nested case-control study, we explored a possible exposure-response relationship between RSC and exposure to RFib or FOR using exposure weighting as an alternative characterization of exposure. Because of the uncertainties in selecting an appropriate exposure-weighting scheme, a range of plausible time lags and unlagged/lagged time windows was considered. As in the initial analysis of the nested case-control study, RFib and FOR exposures were categorized at the deciles of the RSC case distribution. For none of the exposure weighting schemes considered did we observe an increasing RSC risk with increasing levels of RFib_Cum or RFib_AIE. The exposure-weighted estimated risk ratios (RR) for both RFib_Cum and RFib_AIE were generally lower than those obtained from an unweighted model. For FOR_Cum, RRs were generally lower for the time-lagged and unlagged time window models than for the unweighted models, although some decile-specific RRs were higher for the lagged time window models. The exposure-weighted RRs for FOR_AIE were generally lower than the unweighted RRs for all of the weighting schemes considered. This reanalysis in terms of categorized exposures reveals no exposure- response relationships that were undetected in the original analysis where unweighted exposure measures were used. In the schemes considered, exposure weighting generally reduced the estimated risk of RSC.

Code(s): 8, 9, 10.
Chiazze, L. J., D. K. Watkins and C. Fryar. (1997). "Historical cohort mortality study of a continuous filament fiberglass manufacturing plant: I. White men." JOURNAL OF OCCUPATIONAL AND ENVIRONMENTAL MEDICINE; 39 (5). 1997. 432-441. AB - BIOSIS COPYRIGHT: BIOL ABS. An historical cohort mortality study of a continuous filament fiberglass manufacturing plant was undertaken to determine whether an elevated lung cancer risk would be observed on a cohort basis. A nested case-control study of white male lung cancer deaths was incorporated into the study design. An interview survey to obtain information on sociodemographic factors, including smoking, and an historical environmental reconstruction to identify elements in the plant environment to which workers might be exposed were included in the study design. Respirable glass (Beta) fibers were produced only from 1963 to 1968. The lung cancer odds ratio (OR) among those workers exposed to respirable glass fibers is below unity, as are ORs for exposure to asbestos, refractory ceramic fibers, respirable silica (except for the lowest exposure level), total chrome and arsenic. There is a suggestion of an increase with exposure among smokers only for exposure to formaldehyde, although the OR.

Code(s): 8, 9, 10.
Anon. (1996). "Symposium on the health effects of fibrous materials (excluding asbestos) used in industry." The Journal of Occupational Health and Safety - Australia and New Zealand June 1996, Vol.12, No.3, p.243-384. Illus. Bibl.ref.
Proceedings of a symposium held in Sydney, Australia, Oct. 1995. Papers include: evaluation of the potential health risks of man-made fibres; synthetic mineral fibre exposures before and after the Australian national exposure standard and code of practice; mortality among U.S. rock wool and wool slag workers; morbidity following exposure to man-made vitreous fibres; respiratory health of workers in the Australian glass wool and rock wool manufacturing industry; carcinogenicity of synthetic fibres in experimental animals and its significance for workers; toxicity of wool and cellulose fibres; health effects of wollastonite exposure; model for health surveillance for airborne contaminants and respiratory disease in glass wool manufacturing; assessing the biological activity of fibres.

Code(s): 8, 9, 10.
Brooks, S. M. (1995). "Man-Made Mineral Fibers." Environmental Medicine, S. M. Brooks, M. Gochfeld, J. Herzstein, R. J. Jackson, and M. B. Schenker, Editors; Mosby-Year Book, Inc., St. Louis, Missouri, pages 455-461, 90 references, 1995.
A review was conducted of man made vitreous fibers (MMVF), their increasing use as an industrial replacement for asbestos, and their contributions to occupational and environmental pathology. Types of MMVF included mineral wool, glass fiber (glass wool) and refractory ceramic fibers. MMVF exposures in occupational settings were considered, and government standards for exposure were discussed. MMVF size and type have been found to relate to distribution and toxicity. Fiber durability, solubility, chemical composition and surface characteristics have all proven to be important determinants of pathogenicity and cytotoxicity. Human diseases associated with MMVF exposure included cancer, mesothelioma and asbestosis. Exposure duration has been identified as a highly significant factor in assessing the occupational cancer risk associated with MMVF exposure. Human mortality studies and animal inhalation studies were discussed. The author concludes that it is unlikely that nonoccupational exposures would put consumers at substantial risk. Occupational exposures to glass wool and mineral wool may be of more concern with longer duration of exposure. There may be some carcinogenic potential associated with exposure to certain types of ceramic fibers.

Code(s): 8, 9, 10.
De Vuyst, P., P. Dumortier, G. M. Swaen, J. C. Pairon and P. Brochard. (1995). "Respiratory health effects of man-made vitreous (mineral) fibres." Eur Respir J. 8 (12): 2149-73.
The group of man-made mineral or vitreous fibres (MMMFs or MMVFs) includes glass wool, rock wool, slag wool, glass filaments and microfibres, and refractory ceramic fibres (RCFs). Experimental observations have provided evidence that some types of MMVF

are bioactive under certain conditions. The critical role of size parameters has been demonstrated in cellular and animal experiments, when intact fibres are in direct contact with the target cells. It is, however, difficult to extrapolate the results from these studies to humans since they bypass inhalation, deposition, clearance and translocation mechanisms. Inhalation studies are more realistic, but show differences between animal species regarding their sensibility to tumour induction by fibres. Fibre biopersistence is an important factor, as suggested by recent inhalation studies, which demonstrate positive results with RCF for fibrosis, lung tumours and mesothelioma. There is no firm evidence that exposure to glass-, rock- and slag wool is associated with lung fibrosis, pleural lesions, or nonspecific respiratory disease in humans. Exposure to RCF could enhance the effects of smoking in causing airways obstruction. An elevated standard mortality ratio for lung cancer has been demonstrated in cohorts of workers exposed to MMVF, especially in the early technological phase of mineral (rock slag) wool production. During that period, several carcinogenic agents (arsenic, asbestos, polycyclic aromatic hydrocarbons (PAH)) were also present at the workplace and quantitative data about smoking and fibre levels are lacking. It is not possible from these data to determine whether the risk of lung cancer is due to the MMVFs themselves. No increased risk of mesothelioma has been demonstrated in the cohorts of workers exposed to glass-, slag- or rock wool. There are in fact insufficient epidemiological data available concerning neoplastic diseases in RCF production workers because of the small size of the workforce and the relatively recent industrial production.

Code(s): 8, 9, 10.
Plato, N., P. Westerholm, P. Gustavsson, T. Hemmingsson, C. Hogstedt and Krantz. (1995). "Cancer Incidence, Mortality and Exposure-Response among Swedish Man-Made Vitreous Fiber Production Workers." Scandinavian Journal of Work, Environment and Health, Vol. 21, No. 5, pages 353-361, 20 references, 1995.
Workers in three Swedish factories producing man made vitreous fibers (MMVF) were followed up for mortality from 1952 to 1990 and for cancer incidence from 1958 to 1989. The 3,539 workers had been employed at one of the three factories for at least 1 year in MMVF exposed work between the start of production and 1977. The cohort included 1970 workers from a glass wool factory, 1,187 workers from a larger rock wool factory and 382 workers from a smaller rock wool factory. Information on mortality was obtained from a computerized register of the Swedish population. Cause of death was obtained from death certificates. Cancer incidence was obtained from the Swedish Cancer Register. Standardized mortality ratios (SMRs) were calculated. There were 739 deaths in the cohort. There were 27 lung cancer cases, versus 23 expected. There was an observed increased lung cancer risk at the large rock wool factory (SMR 240) and a significantly increased risk of death from external causes (SMR 154) at that factory. There were no other significantly increased mortality risks at the factories. There was a slightly increased lung cancer incidence at the rock wool factories. There was a significantly increased risk of cancer at one of the rock wool factories due to an increased risk for stomach cancer and lung cancer. The possible effect of combustion gas exposure was investigated by creating a subcohort of furnace workers or oven workers who were potentially exposed to polycyclic aromatic hydrocarbons. For this subcohort, the SMR for lung cancer was 131. An exposure/response analysis was conducted for workers at the rock wool factories.

Asbestos and Man-made Vitreous Fibers (MMVFs), non-cancer (1, 2, 3, 8)
—health/irritant effects, metabolism, mechanisms

Code(s): 3, 7, 8.
Brown, D. M., P. H. Beswick, K. S. Bell and K. Donaldson. (2000). "Depletion of glutathione and ascorbate in lung lining fluid by respirable fibres." Ann Occup Hyg. 44 (2): 101-8.
OBJECTIVE: The use of synthetic vitreous fibres has increased along with a decline in the utilisation of asbestos. There remains concern that these synthetic fibres pose a health risk to workers because of the generation of respirable fibres which can enter the lung and cause adverse health effects. An improved understanding of the mechanism of fibre pathogenicity should allow more rational short-term testing regimes for new fibres as they are developed. We hypothesised that carcinogenic fibres have greater free radical activity compared with non-carcinogenic fibres and that they contribute to disease by causing oxidative stress in the lung. We examined a panel of respirable fibres, designated as being carcinogenic or non-carcinogenic based on previous animal studies for ability to deplete antioxidants from lung lining fluid. METHODS: On the basis of inhalation studies, a panel of fibres was divided into three carcinogenic fibres-amosite asbestos, silicon carbide, and refractory ceramic fibre 1 (RCF1) and three non- carcinogenic fibres-man-made vitreous fibre 10 (a glass fibre MMVF10), Code 100/475 glass fibre, and refractory ceramic fibre 4 (RCF4). We measured the levels of glutathione (GSH) and ascorbate, two antioxidants present in lung lining fluid (LLF) after fibre treatment. All of the experiments were carried out at equal fibre number. RESULTS: Fibres had the ability to deplete both GSH and ascorbate from both LLF and pure solutions, an effect which was fibre number dependent. The greatest depletion of antioxidants was observed with the two non- carcinogenic glass fibres, and this effect was observed when A549 lung epithelial cells were treated with fibres. CONCLUSIONS: Our results show that antioxidant depletion in cell free solution and lung lining fluid solely is not a simple indicator of the ability of fibres to cause lung pathology and that other biological events in the lung are involved.

Code(s): 3, 7, 8.

Gulumian, M. (1999). "The role of oxidative stress in diseases caused by mineral dusts and fibres: Current status and future of prophylaxis and treatment." Molecular and Cellular Biochemistry; 196 (1-2). 1999. 69-77.
BIOSIS COPYRIGHT: BIOL ABS. Inhalation of silica and asbestos fibres by humans can lead to fibrosis of the lung and cancer. Different mechanistic approaches, including oxidative stress, are used for prophylactic and therapeutic interventions to attenuate the fibrogenic and carcinogenic effects of these particles. Thus far, most of these therapeutic interventions have been only partly successful. A review of the mechanisms which are thought to be involved in mineral particle-induced toxicity and the relevant therapeutic int

Code(s): 3, 7, 8.
Urano, H., S. Gotoh, A. Shirahata, K. Higashi and Y. Karasaki. (1997). "Increases of Thrombomodulin Activity and Antigen Level on Human Umbilical Vein Endothelial Cells Treated with Asbestos and Man-Made Mineral Fibers." Industrial Health, Vol. 35, No. 3, pages 359-366, 16 references, 1997.
The effects of asbestos (1332214) and man made mineral fibers (MMMF) on the thrombomodulin (TM) activity and antigen levels of human umbilical vein endothelial cells (HUVECs) were examined. Cell cultures were treated with asbestos or MMMF concentrations of 6.25 to 200 micrograms per milliliter (microg/ml) for the cytotoxicity assay, and 0.156 to 10microg/ml for the TM activity and antigen level assays. The incorporation of radiolabeled leucine was determined in cultures exposed to 1microg/ml of crocidolite (12001284) or MMMF. Cell numbers were quantified by the tetrazolium/formazan assay. Dose dependent cytotoxic effects were observed in cells treated with amosite (12172735), crocidolite, and chrysotile (12001295) fibers for 48 hours (hr). At concentrations less than 50microg/ml, toxicity was greatest for chrysotile and lowest for crocidolite. Dose dependent cytotoxic effects were also noted in cells exposed to potassium-titanate (12673697) whisker and magnesium-sulfate (7487889) whisker MMMF for 48hr. At concentrations over 25microg/ml, potassium-titanate whisker was significantly more cytotoxic than magnesium-sulfate whisker. The TM activity of HUVECs treated with crocidolite fibers peaked at 140% of the control value at 1.25microg/ml of crocidolite after 48hr and 2.5microg/ml of crocidolite after 72hr. The TM antigen level peaked at 135 to 145% of the control value at 1.25microg/ml of crocidolite after 48 or 72hr of treatment. In cells treated with 1.25microg/ml of potassium-titanate for 48hr, the TM activity and antigen level peaked at 155% and 143% of the control value, respectively. In cells treated with 2.5 microg/ml of magnesium-sulfate whisker for 72hr, the TM activity and antigen level peaked at 152% and 135% of the control values, respectively. Radiolabeled leucine incorporation increased in HUVECs treated with crocidolite, potassium-titanate, and magnesium-sulfate. The authors conclude that the increases in the TM activity and antigen level may not be induced by the induction of anticoagulant activities, but by the cytotoxic effects of the fibers.

Code(s): 3, 8.
Yatera, K., C. Yoshii, Y. Morimoto, T. Hayashi, T. Imanaga, H. Yamato and M. Kido. (2000). "[A case of pulmonary fibrosis with many asbestos bodies in bronchoalveolar lavage fluid after exposure to asbestos and man-made mineral fibers]." Nihon Kokyuki Gakkai Zasshi. 38 (10): 801-6.
We report a case of severe pulmonary fibrosis in a patient exposed to asbestos and other natural and man-made mineral fibers (MMMF) over a period of time. A 63-year-old man was admitted to our hospital because of progressive dyspnea and severe hypoxemia with hypercapnea. Mineral fibers recovered by bronchoalveolar lavage were analyzed by scanning electron microscope (SEM) and energy-dispersive x-ray spectroscopy (SEM- EDS). The bronchoalveolar lavage fluid (BALF) included a large number of asbestos bodies (116,000/ml). The cores of the asbestos fibers were crocidolite, and no vitreous fibers nor other kinds of man-made mineral fibers (MMMFs) were identified. To our knowledge, the number of asbestos bodies per ml of this patient's BALF is the greatest ever reported. Insufficient personal protection of the airways, high concentrations of inhaled fibers, co-exposure to cigarette smoke, and prolonged biopersistence of crocidolite asbestos fibers are presumed to be the causes of such severe asbestosis.

Code(s): 3, 8.
Hurbankova, M. and A. Kaiglova. (1997). "Effect of occupational and environmental exposure to industrial fibrous dusts on the respiratory tract." Biologia (Bratislava); 52 (3). 1997. 431-439.
BIOSIS COPYRIGHT: BIOL ABS. Biological effects of asbestos and other industrial mineral fibres were compared after occupational exposure of men, in an in vivo experiment on animals, and on in vitro cell cultures. Some immunologic and cytotoxic factors in workers as well as in experimental animals exposed to asbestos (crocidolite, amosite, chrysotile) and asbestos substitutes (basalt, glass fibres, wollastonite) were evaluated in comparison with a control group. The parameters determined in blood were immunoglobulins A, G, and M, complement components C3, C4, alpha-1-antitrypsin, transferrin, and the number and phagocytic activity of leukocytes. In bronchoalveolar lavage (BAL) total cell number and the number of AM per ml of BAL fluid, the AM to granulocyte ratios, phagocytic activity of AM, the levels of lactate dehydrogenase and acid phosphatase, as well as the in vitro chemiluminescent activity of AM were investigated. Our results confirmed the adverse reactions of asbestos fibres. The mechanism

Code(s): 3, 8.

Uthman, M. O., T. Goltsova, S. D. Brown and R. F. Hamilton, Jr. (1997). "Asbestos and Silica-Induced Changes in Human Alveolar Macrophage Phenotype AU - Holian A." Environmental Health Perspectives, Vol. 105, Supplement 5, pages 1139-1142, 20 references, 1997.
In order to test the hypothesis that fibrogenic particulates such as asbestos (1332214) and silica could affect the phenotype ratio of human alveolar macrophages (AM) in-vitro, human AM were incubated with chrysotile (12001295), crocidolite (12001284), crystalline silica (14808607), wollastonite (13983170), and titanium-dioxide (13463677) and then examined by flow cytometry for changes in expression of RFD1 and RFD7 surface markers. AM from normal, nonsmoking adults were cultured for 4 or 24 hours without particulates, or with 25 micrograms/milliliter (microg/ml) chrysotile, 75microg/ml crocidolite, 133microg/ml silica, 60microg/ml titanium-dioxide, or 200microg/ml wolastonite. Concentrations were selected to provide approximately the same particulate surface area. The PFD1+ phenotype was increased and the RFD1+RFD7+ phenotype was decreased by exposure to chrysotile, crocidolite and silica, but not by exposure to titanium-dioxide or wollastonite. The authors suggest that their findings provide a mechanistic explanation that may link apoptosis to a shift in the ratio of macrophage phenotypes that could initiate lung inflammation. Fibrogenetic particulates may be able to cause a shift in macrophage phenotypes to a more inflammatory condition without having to induce inflammation by themselves. If so, this indicates that new approaches to therapy need to be explored, with agents that could restore the normal phenotype balance and ablate the progressive inflammatory conditions in fibrosis.

Code(s): 3, 8.
Hill, I. M., P. H. Beswick and K. Donaldson. (1996). "Enhancement of the macrophage oxidative burst by immunoglobulin coating of respirable fibers: fiber-specific differences between asbestos and man-made fibers." Exp Lung Res. 22 (2): 133-48.
The ability of long amosite asbestos fibers (LFA), vitreous fibers (MMVF 21 and CODE 100/475), and ceramic fibers (silicon carbide and RCF 1) to stimulate superoxide production in isolated rat alveolar macrophages is examined. The cells were exposed to both naked fibers (uncoated) and fibers coated with rat immunoglobulin (IgG), a normal component of lung lining fluid. The affinity for IgG of the various fibers was assessed by quantifying the binding of 125I-labeled IgG onto the fiber surface. Naked fibers stimulated a modest release of superoxide anion from alveolar macrophages, which was not obviously dose dependent. When IgG was adsorbed onto fibers of MMVF 21 and RCF 1, there was a dramatic increase in superoxide release, which correlated well with their high affinity for IgG.IgG-adsorbed code 100/475 and silicon carbide whiskers (SiCW) stimulated only modest superoxide release, and the fibers showed a correspondingly poor affinity for the opsonin. Conversely, the adsorbed fibers of LFA, generated a dramatic increase in superoxide release from the macrophages, despite a relatively poor adsorption of IgG. This study demonstrates the potential for components of the lung lining fluid to modify the response of alveolar macrophages to respirable natural and man-made fibers. It also draws attention to fiber-specific differences in adsorptive capacity and subsequent biological activity between these fiber types in vitro and, by implication, in vivo.

Code(s): 3, 8, 15.
Anon. (1995). "Toxicity of Fibers. (Latest citations from the Energy Science and Technology Database)." Govt Reports Announcements & Index (GRA&I), Issue 19, 1995.
TD3: The bibliography contains citations concerning the sources and toxicity of natural and synthetic fibers. Topics include indoor air pollution, fibrous dust control, toxicity of insulation materials, chronic inhalation studies, and respiratory diseases. Industrial monitoring systems and asbestos fiber in drinking water are examined. (Contains 50-250 citations and includes a subject term index and title list.) Published Search. Updated with each order. Supersedes PB94-860608. Prepared in cooperation with Department of Energy, Washington, DC. Sponsored in part by National Technical Information Service, Springfield, VA.

Asbestos and Man-made Vitreous Fibers (MMVFs), cancer (4, 5, 6, 9)
—health/irritant effects, metabolism, mechanisms

Code(s): 6, 9.
Vasama-Neuvonen, K., E. Pukkala, H. Paakkulainen, P. Mutanen, E. Weiderpass, P. Boffetta, N. Shen, T. Kauppinen, H. Vainio and T. Partanen. (1999). "Ovarian cancer and occupational exposures in Finland." Am J Ind Med. 36 (1): 83-9.
BACKGROUND: No single occupational or environmental agent has been established as causing ovarian cancer, existing studies often being based on ecologic or proportional mortality data in which potential confounders related to reproductive history have not been taken into account. METHODS: This study linked 324 job titles of occupationally active Finnish women (n = 892,591) at 1970 census with incidence of ovarian cancer (Finnish Cancer Registry, 5,072 cases) during 1971-1995 (over 15 million person-years). The job titles were converted into indicators of exposure to 33 agents, using a national job-exposure matrix based on measurements and surveys (FINJEM). Poisson regression analyses were performed with stratification by birth cohort, follow-up period, and socioeconomic status, and adjusted for mean number of children, mean age at first delivery, and turnover rate for each job title. RESULTS: We found indications of elevated risks for aromatic hydrocarbon solvents (standardized incidence ratio 1.3 (95% CI 1.0-1.7), leather dust (1.4; 0.7-2.7), man-made vitreous fibers (1.3; 0.9- 1.8), and high levels of asbestos (1.3; 0.9-1.8), and diesel (1.7; 0.7-

4.1), and gasoline (1.5; 1.0-2.0) engine exhausts). Previously reported findings for hairdressers and women in the printing industry were supported in our data, but not for women in dry cleaning jobs. CONCLUSIONS: Given the various drawbacks in linkage studies and job- exposure matrices, the excesses found in this study need confirmation in individual-level studies.

Code(s): 6, 9.
Weiderpass, E., E. Pukkala, T. Kauppinen, P. Mutanen, H. Paakkulainen, K. Vasama-Neuvonen, P. Boffetta and T. Partanen. (1999). "Breast cancer and occupational exposures in women in Finland." Am J Ind Med. 36 (1): 48-53.
BACKGROUND: The etiology of breast cancer is not fully understood. Environmental and occupational exposures may contribute to breast cancer risk. METHODS: We linked 324 job titles from the 1970 census of 892,591 Finnish women with incidence of breast cancer (23,638 cases) during 1971-1995. We converted job titles to 31 chemical and two ergonomic agents through a measurement-based, period-specific, national job-exposure matrix. Poisson regression models were fit to the data, with adjustment for birth cohort, follow-up period, socioeconomic status, mean number of children, mean age at first delivery, and turnover rate. RESULTS: For premenopausal breast cancer, medium/high level of occupational exposure to ionizing radiation was associated with a standardized incidence ratio (SIR) of 1.3 (95% confidence interval (CI) 0.7-2.5; trend P = 0.03). For postmenopausal breast cancer, we found on SIR of 1.2 (1.1-1.3) for low level and 1.4 (1.1- 1.8) for medium/high level of ionizing radiation (trend P = 0.001); and an SIR 1.3 (1.1-1.7) for medium/high levels of both asbestos and man- made vitreous fibers. Aromatic hydrocarbon solvents showed a significant trend for a modest excess of postmenopausal breast cancer. CONCLUSIONS: Our study indicates that occupational exposure to ionizing radiation may be associated with an increased risk of female breast cancer. High-quality studies on environmental and occupational etiology of breast cancer are needed for further elucidation of risk factors.

Code(s): 6, 9.
Dopp, E., M. Schuler, D. Schiffmann and D. A. Eastmond. (1997). "Induction of micronuclei, hyperdiploidy and chromosomal breakage affecting the centric/pericentric regions of chromosomes 1 and 9 in human amniotic fluid cells after treatment with asbestos and ceramic fibers." Mutat Res. 377 (1): 77-87.
This article describes the induction of micronuclei, hyperdiploidy and chromosome breakage in human amniotic cells in vitro by amosite, chrysotile and crocidolite asbestos, and ceramic fibers. The response of human (amniotic fluid cells) and rodent (Syrian hamster embryo fibroblasts, SHE) cells to fiber treatment was compared using the micronucleus assay. The data of the rodent studies were taken from a previous investigation (Dopp, E. et al. (1995) Environ. Health Perspect., 103, 268-271). All types of mineral fibers caused a significant increase of micronucleated cells. The kinetochore analysis revealed that all three types of asbestos and ceramic fibers yielded similar effects. Approximately 50% of the induced micronuclei were kinetochore-negative indicating formation through clastogenic events. Human amniotic cells were much less susceptible than SHE cells to the induction of micronuclei by mineral fibers. This again demonstrates that SHE cells are more susceptible to chromosomal changes than human amniotic fluid cells. The application of fluorescence in situ hybridization (FISH) with tandem DNA probes yielded more detailed information about specific structural chromosome aberrations in the 1 (cen-q12) and 9 (cen-q12) regions and about abnormal numbers of chromosomes in interphase human amniotic fluid cells. Using this FISH approach we found a statistically significant increase of chromosomal breakage in the pericentric heterochromatin regions of chromosomes 1 and 9 in interphase human amniotic cells after exposure to asbestos and ceramic fibers compared to control cells. The number of hyperdiploid cells was also significantly increased. Our results show that asbestos fibers as well as ceramic fibers are inducers of structural and numerical chromosomal aberrations in human amniotic fluid cells.

Code(s): 6, 9.
Husgafvel-Pursiainen, K., A. Kannio, P. Oksa, T. Suitiala, H. Koskinen, R. Partanen, K. Hemminki, S. Smith, R. Rosenstock-Leibu and P. W. Brandt-Rauf. (1997). "Mutations, tissue accumulations, and serum levels of p53 in patients with occupational cancers from asbestos and silica exposure." Environ Mol Mutagen 1997;30(2):224-30.
In order to determine the relationship between mutations, tissue accumulations, and serum levels of p53 in occupational cancers, we used denaturing gradient gel electrophoresis and DNA sequencing of exons 5-9 of the p53 gene, immunohistochemical analysis for tissue identification of mutant p53 protein, and enzyme-linked immunosorbent assay for serum levels of mutant p53 protein to examine for such alteration in a cohort of individuals with workplace exposure to asbestos or silica, and resultant lung cancers or mesotheliomas. DNA analysis detected mutations in 5 of 18 (28%) tumors, and tissue accumulations of protein were detected in 7 of 20 (35%) tumors; the agreement between mutational and immunohistochemical analyses was significant (kappa = 0.62, P = 0.002). Serum elevations of protein were detected in 4 of 11 (36%) cases with available serum samples; the agreement between tissue alterations and serum elevations was also significant (kappa = 0.71, P = 0.017). In addition, based on the analysis of banked samples, serum results tended to be consistent over time prior to the diagnosis of disease (positive predictive value = 0.67, negative predictive value = 0.83). These results suggest that serum levels of p53 are reasonably accurate in reflecting tissue alterations in p53 at the gene and/ or protein level and may be early biomarkers of disease risk.

Code(s): 6, 9.

Johnson, N. F. and R. J. Jaramillo. (1997). "p53, Cip1, and Gadd153 expression following treatment of A549 cells with natural and man-made vitreous fibers." Environ Health Perspect. 105 Suppl 5 1143-5.
DNA damage induced by chemicals and ionizing radiation is associated with the expression of negative regulators of the cell cycle. The arrest of cells in G1 and G2 phases of the cell cycle provides time for DNA repair. Asbestos fibers are carcinogenic when inhaled by both humans and animals; however, the mechanism by which the fibers exert their effect is unknown. This work was undertaken to determine whether the expression of DNA damage-inducible genes differs between crocidolite, a fiber positive for lung tumors, and JM 100 glass microfiber, which is negative for lung tumors when inhaled by rats. Temporal and dose-related expressions of p53, Cip1, and Gadd153 proteins were determined in cultured A549 cells treated with either Union Internationale Contre le Cancer crocidolite or JM 100 for 20 hr and cultured in fresh media. Immunolabeled cells were analyzed by flow cytometry, and the increased number of protein-expressing cells was determined by subtracting the expression in unexposed cells from exposed cells. Crocidolite induced the expression of all three proteins with a maximum expression after approximately 18 hr in fresh media. At a similar time point, JM 100 did not markedly induce the three proteins. Crocidolite also induced a dose-dependent increase in the number of cells in the G2 phase of the cell cycle. These results show that asbestos behaves like ionizing radiation and genotoxic chemicals by inducing proteins associated with DNA damage and cell-cycle arrest. The clear difference in response between crocidolite and JM 100 may help elucidate the mechanism of action of toxic and nontoxic fibers.

Code(s): 6, 9.
Howden, P. J. and S. P. Faux. (1996). "Glutathione modulates the formation of 8-hydroxydeoxyguanosine in isolated DNA and mutagenicity in Salmonella typhimurium TA100 induced by mineral fibres." Carcinogenesis. 17 (10): 2275-7.
Treatment of isolated DNA with crocidolite and man-made vitreous fibre- 21 (MMVF-21) significantly increased the concentration of 8- hydroxydeoxyguanosine (8-OHdG) in isolated DNA above background levels and co-treatment with glutathione (GSH) eliminated this effect. Crocidolite, MMVF-21 and chrysotile fibres increased the number of revertants in Salmonella typhimurium TA100 and GSH-deficient strains, TA100/NG-54 and TA100/NG-57, over background levels. This increase was small in TA100 but was greater in the GSH-deficient strains. When these bacterial strains were further depleted of GSH by co-culture with buthionine sulfoximine, all fibres tested caused a significant increase in the number of revertants over the parent strains. Pre-treatment with the GSH precursor N-acetyl-L-cysteine reduced the number of revertants to below that of the parent strain. Previous studies have shown a mechanistic role for iron-catalyzed production of oxygen radicals in the mutagenicity of fibres and this study suggests a protective role for GSH against such oxidative damage possibly by acting as a radical scavenger.

Code(s): 6, 9.
Howden, P. J. and S. P. Faux. (1996). "Fibre-induced lipid peroxidation leads to DNA adduct formation in Salmonella typhimurium TA104 and rat lung fibroblasts." Carcinogenesis. 17 (3): 413-9.
Certain end-products of lipid peroxidation bind to DNA forming a fluorescent chromophore. Incubation of both Salmonella typhimurium TA104 and a rat lung fibroblast cell line, RFL-6, with various types of mineral fibre resulted in a time- and dose-dependent increase in DNA fluorescence. The increase in DNA fluorescence was shown to be directly related to the amount of iron that could be mobilized from the fibre surface using in vitro studies in the absence of cells or bacteria. Crocidolite and man-made vitreous fibre-21 (MMVF-21) mobilized significant quantities of iron and were significantly more active than chrysotile and refactory ceramic fibre-1 (RCF-1). Fibre-induced malondialdehyde-DNA adduct formation, the fluorescent product, was increased by incubating cells with buthionine sulfoximine and ameliorated by co-treatment with N-acetylcysteine, indicating a protective role for glutathione. Similarly, vitamin E was also shown to inhibit DNA adduct formation. These results suggest that mineral fibre- induced lipid peroxidation produced genotoxic products which can diffuse into nucleus and interact with cellular DNA. In conclusion, fibre-induced lipid peroxidation may be a possible mechanism in the genotoxic action of fibrous materials.

Code(s): 6, 9.
Donaldson, K., P. S. Gilmour and P. H. Beswick. (1995). "Supercoiled plasmid DNA as a model target for assessing the generation of free radicals at the surface of fibres." Exp Toxicol Pathol. 47 (4): 235-7.
The ability of respirable amosite and crocidolite asbestos, refractory ceramic fibres (RCFs) and man made vitreous fibres (MMVFs) to cause free radical injury to plasmid, phiX174 RFI DNA was assessed. The amosite and crocidolite asbestos caused substantial damage to the DNA and, in the main, the free radicals responsible for the asbestos- mediated DNA damage were hydroxyl radicals as determined by inhibition with mannitol. Asbestos fibre-mediated damage to the DNA was completely ameliorated by the chelation of fibre-associated iron by pre-treatment of fibres with desferrioxamine-B, confirming the importance of iron in the production of free radicals. MMVFs and RCFs produced modest free radical damage to the DNA, which was prevented by mannitol but not by iron chelation.

Code(s): 6, 9.
Kamp, D. W., V. A. Israbian, S. E. Preusen, C. X. Zhang and S. A. Weitzman. (1995). "Asbestos causes DNA strand breaks in

cultured pulmonary epithelial cells: role of iron-catalyzed free radicals." Am J Physiol 1995 Mar;268(3 Pt 1):L471-80.
Asbestos causes pulmonary fibrosis and various malignancies by mechanisms that remain uncertain. Reactive oxygen species in part cause asbestos toxicity. However, it is not known whether asbestos-induced free radical production causes alveolar epithelial cell (AEC) cytotoxicity by inducing DNA strand breaks (DNA-SB). We tested the hypothesis that asbestos-induced AEC injury in vitro is due to iron-catalyzed free radical generation, which in turn causes DNA-SB. We found that amosite asbestos damages cultured human pulmonary epithelial-like cells (WI-26 cells) as assessed by 51Cr release and that an iron chelator, phytic acid (500 microM), attenuates these effects. A role for iron causing these effects was supported by the observation that ferric chloride-treated phytic acid did not diminish WI-26 cell injury. Production of hydroxyl radical-like species (.OH) was assessed based upon the .OH-dependent formation of formaldehyde (HCHO) in the presence of dimethyl sulfoxide. A variety of mineral dusts induced significant levels of .OH formation (nmol HCHO at 30 min: carbonyl iron, 85 +/- 21; amosite asbestos, 14 +/- 2; chrysotile asbestos, 7 +/- 1; titanium dioxide, 2.5 +/- 0.5). Phytic acid significantly diminished the asbestos-induced .OH production. DNA damage to AEC was assessed by the alkaline unwinding, ethidium bromide fluorometric technique. Hydrogen peroxide caused dose-dependent DNA-SB in WI-26 cells after a 30-min exposure period [50% effective dose (ED50): 5 microM] that was similar to other cell lines. Amosite asbestos induced dose-dependent DNA-SB in WI-26, A549, and primary isolated rat alveolar type II cells maintained in culture for 7-10 days (alveolar type I-like). Lower doses of amosite (0.5-5 micrograms/ml or 0.25-2.5 micrograms/cm2) caused significant WI-26 cell DNA-SB after prolonged exposure periods (cultured AEC. There was a direct correlation between mineral dust-induced .OH production at 30 min and DNA-SB in WI-26 cells at 4 h ($P < 0.0005$). These data suggest that mineral dusts can be directly genotoxic to relevant target cells of asbestos, AEC. Furthermore, these results provide additional support for the premise that iron-catalyzed free radicals mediate asbestos-induced pulmonary toxicity.

Code(s): 6, 9, 14, 15.
Berry, G. (1999). "Models for mesothelioma incidence following exposure to fibers in terms of timing and duration of exposure and the biopersistence of the fibers." Inhal Toxicol. 11 (2): 111-30.
The health effects of inhaled fibers are related to the intensity and duration of exposure and occur many years after the exposure. In particular, the incidence of mesothelioma after exposure to asbestos is proportional to the intensity of exposure (fibers per milliliter of air) and the duration of exposure, and to the time that has elapsed since the exposure. The incidence increases with time since exposure to a power of between 3 and 4. The disease process resulting from exposure to fibers in the air is presumably related to the dose of fibers in the lungs, which depends on the exposure level and duration, and also on the size characteristics of the fibers influencing their inhalation and retention in the lungs. Models incorporating these characteristics have been found to be satisfactory in explaining the incidence of mesothelioma over time after exposure to asbestos. Most of the epidemiological modeling has been for occupational exposure to one of the amphibole asbestos types (crocidolite or amosite), for which heavy exposure produces a high incidence of mesothelioma. Occupational exposure to chrysotile asbestos has resulted in a much lower incidence of mesothelioma. Crocidolite asbestos is much more biopersistent than chrysotile asbestos in the sense that after retention in the lungs it is eliminated only slowly (half-time of several years). If fibers are eliminated then the dose in the lungs declines following exposure, and this may influence the disease process. This concept is more important for synthetic mineral fibers, such as glass wool, which are used as a substitute for asbestos. These fibers are much less biopersistent than asbestos, with half-times of weeks or even days. Biopersistence is related to the dissolution of fibers. This is a physical-chemical process that may be expected to proceed at about the same rate in rats and humans. The predicted effect of biopersistence of fibers has been explored using the basic mesothelioma incidence model generalized to include a term representing exponential elimination over time. The influence of solubility of fibers on the mesothelioma rate is 17 times higher in humans than in rats. This is because rats are aging and developing cancer at a much quicker rate than humans, and hence the influence of dissolution is less. Thus, the predicted mesothelioma incidence in humans is highly dependent on the rate of elimination across the range covering asbestos and the more durable synthetic fibers, but in rats a similar dependence occurs at a 17 times higher rate of elimination corresponding to the less durable synthetic fibers. The possible carcinogenic effects of fibers are often determined from animal experiments, but these results suggest that the extrapolation from rats to humans is highly dependent on the biopersistence of fibers, in the situation where the elimination is through dissolution of fibers at a rate independent of species and the speed of the cancer process is species dependent. This implies that relatively soluble fibers that do not produce disease in rat experiments are even less likely to produce disease in humans.

Man-made Vitreous Fibers (MMVFs), exposures (11)
—exposure levels, fiber size, no health effects

Code(s): 11.
Longo, W. E., W. B. Egeland, R. L. Hatfield and L. R. Newton. (2002). "Fiber release during the removal of asbestos-containing gaskets: a work practice simulation." Appl Occup Environ Hyg. 17 (1): 55-62.
Work practice studies were conducted involving the removal of asbestos- containing sheet gaskets from steam flanges. These studies were performed to determine potential exposure levels to individuals who have worked with these types of materials in the past and may still work with these products today. The work practices were conducted inside an exposure characterization laboratory (ECL) and were performed by scraping and wire brushing, chrysotile-containing (65% to 85%) sheet gaskets from a number of used steam flanges. Airborne asbestos levels were measured by phase contrast microscopy (PCM) and transmission electron microscopy (TEM) for the personnel and area air samples collected during the study. These workplace simulations showed substantial asbestos fiber release using scraping, hand wire brushing, and power wire brushing techniques during the gasket removal process. The range of concentration was 2.1 to 31.0 fibers/cc greater than 5 micrometers when measured by PCM. These results contrasted with the few reported results in the published literature where lower airborne asbestos levels were reported. In these studies the airborne asbestos fiber levels measured in many of the samples exceeded all current and historical Occupational Safety and Health Administration (OSHA) excursion limits (15-30 minutes) and some previous permissible exposure limits (PEL) based on eight-hour time-weighted average (TWA) standards. Also, individuals who performed this type of work in the past may have had exposures higher than previously suspected. The results demonstrated that employees who remove dry asbestos-containing gaskets with no localized ventilation should wear a full face supplied air respirator with a HEPA escape canister and the work area should be designated a regulated area.

Code(s): 11.
Camilucci, L., A. Campopiano, S. Casciardi, F. Fioravanti and D. Ramires. (2001). "[Exposure to artificial mineral fibers in public buildings]." Med Lav. 92 (1): 32-8.
Man-made mineral fibers are widely used as asbestos substitutes in many application fields. Therefore toxicology studies and indoor pollution surveys, related to man-made mineral fibers, are becoming very important. Several surveys were made in office buildings where the main source of indoor pollution was the dispersion of man-made mineral fibers contained in the insulation materials (under-ceiling panels, partitions and material used in air-conditioning installations). Samples of the insulation materials were taken and analyzed by phase contrast optical microscopy and scanning electron microscopy equipped with energy-dispersive X-ray analysis. For some samples the fiber diameter measurements were made and the related statistical parameters were calculated. The measured airborne fiber concentrations showed non relevant man-made mineral fiber dispersion in the environment. The relative exposure limits and regulations in force are discussed.

Code(s): 11.
MacKinnon, P. A., T. J. Lentz, C. H. Rice, J. E. Lockey, G. K. Lemasters and P. S. Gartside. (2001). "Electron microscopy study of refractory ceramic fibers." Appl Occup Environ Hyg. 16 (10): 944-51.
In epidemiological studies designed to identify potential health risks of exposures to synthetic vitreous fibers, the characterization of airborne fiber dimensions may be essential for assessing mechanisms of fiber toxicity. Toward this end, air sampling was conducted as part of an industry-wide study of workers potentially exposed to airborne fibrous dusts during the manufacture of refractory ceramic fibers (RCF) and RCF products. Analyses of a subset of samples obtained on the sample filter as well as on the conductive sampling cowl were performed using both scanning electron microscopy (SEM) and transmission electron microscopy (TEM) to characterize dimensions of airborne fibers. Comparison was made of bivariate fiber size distributions (length and diameter) from air samples analyzed by SEM and by TEM techniques. Results of the analyses indicate that RCF size distributions include fibers small enough in diameter (< 0.25 microm) to be unresolved by SEM. However, longer fibers (> 60 microm) may go undetected by TEM, as evidenced by the proportion of fibers in this category for TEM and SEM analyses (1% and 5%, respectively). Limitations of the microscopic techniques and differences in fiber-sizing rules for each method are believed to have contributed to the variation among fiber-sizing results. It was concluded from these data that further attempts to characterize RCF exposure in manufacturing and related operations should include analysis by TEM and SEM, since the smallest diameter fibers are not resolved with SEM and the fibers of longer length are not sized by TEM.

Code(s): 11.
Marconi, A., F. Cavariani, A. Carai, G. Cacchioli, F. Papandrea and E. Cacchioli. (2001). "[Assessment of exposure to ceramic fibers during insulation operations in a thermoelectric power plant]." Med Lav. 92 (4): 263-71.
Refractory ceramic fibre concentrations were measured during renewal of the insulation lining of a turbine located in a large power plant. Personal and stationary samples were collected during operations, which involved installing and ripping out standard and

pre-coated and pre- shaped ceramic fibre blankets. Operation-length average (OLA) and TWA exposure levels were about 500 F/l and about 100 F/l, respectively, for installing and ripping out operations where non-coated blankets were handled. In these cases specific task-associated personal exposure levels up to 1000 F/l were measured. Personal exposure levels up to as much as 10 times lower were observed in operations involving pre-coated and pre-shaped blankets. The average concentration levels from area samples were always lower than those from personal samples, and showed a downward gradient with the distance from the source. Given the current carcinogenic classification of refractory ceramic fibres (class 2, European), the necessity is stressed of introducing adequate working practices and control measures (adoption of pre-coated and pre-shaped fibrous materials whenever possible, confinement of working area, use of local air extractions ventilation with HEPA filter unit, use of garments for personal protection and respirators, use of wetting or binding liquids prior to removal, quick cleaning of debris from working area), in order to keep the exposure levels and the number of potentially exposed workers to the minimum.

Code(s): 11.
Besson, P., F. X. Lalanne, Y. Wang and F. Guyot. (1999). "Multi-parameter observation of environmental asbestos pollution at the Institut de Physique du Globe de Paris (Jussieu Campus, France)." Ann Occup Hyg. 43 (8): 527-41.
An original multi-parameter system has been used to study the nature of dust in the ambient air, particularly the total fibers and asbestos fibers, in eight areas of the Institut de Physique de Globe de Paris (France). These analyses provide a detailed case study of environmental pollution by asbestos fibers at low levels. The levels of total fibers with a length greater than 3 microns, measured with a real time fiber analyser monitor (FAM), give a baseline of 2.5 fibers per l., throughout the duration of sampling. The same levels, calculated during periods of effective presence of staff, are smaller than 10 fb per l. During these periods, the instantaneous value can show high peaks, reaching a maximum of 60 fb per l., but more often of about 5 to 10 fb per l. A direct cause and effect relationship exists between fiber concentrations and the presence of people, and indirectly with the variation of the other environmental parameters (temperature, humidity, air velocity). The baseline concentration of asbestos fibers, determined by analytical transmission electron microscopy (ATEM), is about 10(-1) fb per l., with a mean value during the presence of people always less than 1.5 fb per l. The low levels of asbestos fibers do not allow us to establish a precise correlation between the concentration of total fibers and the asbestos concentration, but a rough estimate suggests that asbestos could represent 10-20% of the airborne fibers monitored with the FAM. The statistical study of fiber sizes shows that 70 and 55% of analyzed chrysotile and amosite fibers respectively are smaller than 5 microns. These numbers are 40 and 35% for fibers smaller than 3 microns, which are undetected by the FAM. Amosite, which characterizes most of the asbestos-containing materials (ACM) in the analyzed areas, is detected in the ambient air in quantities ten times less important than chrysotile. The low asbestos levels and the difference between the nature of building asbestos and airborne fibers, show that the mean measured asbestos contents in the ambient air represent the geochemical background of chrysotile asbestos fibers in the Parisian air.

Code(s): 11.
Kim, J. H., H. S. Chang, K. Y. Kim, W. M. Park, Y. J. Lee, H. C. Choi, K. A. Kim and Y. Lim. (1999). "Environmental measurements of total dust and fiber concentration in manufacturer and user of man-made mineral fibers." Ind Health. 37 (3): 322-8.
Man-made mineral fibers (MMMF), most of which are referred to as man- made vitreous fibers (MMVF), are mostly amorphous silicates manufactured from glass, rock, or other minerals. Analysis for MMMF have been restricted largely to the measurement of total airborne mass concentrations, but more recently to the determination of airborne fiber levels by phase contrast optical microscopy. In Korea, many small factories are related with manufacturing and using MMMF without any special evaluation of environmental measurements. Though MMMF are known as the substitute of asbestos and their toxicity are regarded as very low, MMMF do not totally excluded from the respiratory and/or skin diseases now. Therefore, we evaluated the environments of many workplaces with total dust and fiber concentration. Most dust and fiber concentrations were below threshold limit value (TLV) at various industries and working processes. However, these data showed a slight relationship between total dust and fiber concentration.

Code(s): 11.
Lentz, T. J., C. H. Rice, J. E. Lockey, P. A. Succop and G. K. Lemasters. (1999). "Potential significance of airborne fiber dimensions measured in the U.S. refractory ceramic fiber manufacturing industry." Am J Ind Med. 36 (2): 286-98.
BACKGROUND: To determine dimensions of airborne fibers in the U.S. refractory ceramic fiber (RCF) manufacturing industry, fibers collected through personal air sampling for employees at RCF manufacturing and processing operations have been measured. METHODS: Data were derived from transmission electron microscopy analyses of 118 air samples collected over a 20-year period. RESULTS: Characteristics of sized fibers include: diameter measurements of <60; 0.19 to 1.0 micron, m of which 75% are less than 0.6 micron and length ranging from < 0.6 to > 20 micron, with 68% of fibers between 2.4 and 20 micron. CONCLUSIONS: Exposures in RCF manufacturing include airborne fibers with dimensions (diameter < 0.1-0.4 micron, length < 10 micron) historically associated with biological effects in pleural tissues. Air sampling data and a review of studies relating fiber size to pleural effects in animals and humans support the belief that information on fiber dimensions is essential for studies with synthetic vitreous fibers.

Code(s): 11.
Pastuszka, J. S., A. Kabala-Dzik and K. T. Paw. (1999). "A study of fibrous aerosols in the home environment in Sosnowiec, Poland." Sci Total Environ. 229 (1-2): 131-6.
This work constitutes the first report on the concentration of airborne respirable fibers, and their length distribution in different groups of homes in Sosnowiec, Poland. The measurements have been made by using the MIE Laser Fiber Monitor FM-7400. Mean concentration level of the respirable fibers, longer than 5 microns, ranged from 350 m-3 through 910 m-3 up to 1020 m-3 in the homes located in suburban areas, near the busy streets, and in the buildings covered with asbestos-cement sheets, respectively. These results indicate the outdoor asbestos-containing materials as the main sources of airborne fibers inside the Sosnowiec dwellings.

Code(s): 11.
Spencer, J. W., M. J. Plisko and J. L. Balzer. (1999). "Asbestos fiber release from the brake pads of overhead industrial cranes." Appl Occup Environ Hyg. 14 (6): 397-402.
The purpose of this evaluation was to determine the actual contribution of airborne asbestos fibers to the work environment from the operation of overhead cranes and hoists that use asbestos composition brake pads. The evaluation was conducted in a working manufacturing facility. Other potential sources of asbestos were accounted for by visual inspection and background air monitoring. An overhead crane assembly comprised of a trolley and two hoists was employed for this study. The crane was operated for two consecutive eight-hour shifts representative of a heavy-duty cycle. Forty-four personal and area air samples were collected during the assessment. Asbestos fibers were analyzed for by phase contrast (NIOSH 7400), and transmission electron (NIOSH 7402) microscopy methods. Eight-hour time-weighted average (TWA) asbestos fiber concentrations ranged from < 0.005 to 0.011 fibers/cc (PCM), and < 0.0026 to < 0.0094 f/cc (TEM). There were no asbestos fibers detected by the TEM method from air samples collected during the operation of the cranes.

Code(s): 11.
Burdett, G. (1998). "A comparison of historic asbestos measurements using a thermal precipitator with the membrane filter-phase contrast microscopy method." Ann Occup Hyg. 42 (1): 21-31.
The published results and analytical methods used in a 1938 survey of the spinning area in a UK crocidolite asbestos factory have been described and re-interpreted, by comparing the method used with the current membrane filter-phase contrast microscopy (MF-PCM) method for asbestos. By good fortune, most of the original microscope, and thermal precipitator sampling heads similar to those used for sampling were available, as well as guidance from the factory inspector who collected and analysed the original samples. A textile grade crocidolite asbestos was used to generate a fibrous dust cloud whose size distribution was characterised by scanning and transmission electron microscopy and found to give a close approximation to the fibre size distributions monitored in 1938. Samples taken over the same sampling time, but at lower concentrations than originally sampled, showed that the thermal precipitator-oil immersion microscopy (TP-OI) method used at x 2000 magnification, gave higher > 5 microns long fibre counts by a factor of between 3 and 4, than the current MF-PCM method. The differences in performance could be explained by the superior resolving power of the TP-OI method for fine crocidolite fibres. Exposures of airborne asbestos fibres in the spinning area were found to be equivalent to about 20 f ml-1 for personal samples and 10 f ml-1 for area samples, but due to the high levels of ventilation on the day the samples were collected, the average levels throughout the year may have been somewhat higher.

Code(s): 11.
Alderisio, M., M. R. Giovagnoli, M. Cenci and A. Vecchione. (1996). "Asbestos bodies in the sputum of workers exposed to environmental pollution." Anticancer Research; 16 (5a). 1996. 2965-2968.
BIOSIS COPYRIGHT: BIOL ABS. The diseases related to asbestos exposure (pulmonary fibrosis, broncogenic carcinoma and mesothelioma) are of widespread interest and involve different socioeconomic groups of subjects. Since these pathologies have a wide diffusion in the industrial world, we carried out an investigation on two populations occupationally exposed to air pollution and asbestos fibre inhalation (164 traffic policemen of the municipal district of Rome and 218 railwaymen) and on a control group (119 residents in a rural district of Perugia) for the detection of asbestos bodies in the sputum. The results obtained from traffic policemen and railwaymen workers differed significantly from those of the control group. The presence of asbestos bodies in traffic policemen seems to be determined by a strong synergetic effect between gaseous urban pollution, cigarette smoking habits and asbestos dust arising from car brakes and building materials, whereas, in railwaymen it seems to be more directly co

Code(s): 11.
De Rosa, E., M. Cellini, G. Sessa, M. L. Scapellato, G. Marcuzzo and G. B. Bartolucci. (1996). "The Importance of Sampling Time and Coexposure to Acetone in the Biological Monitoring of Styrene-Exposed Workers." Applied Occupational and Environmental Hygiene, Vol. 11, No. 5, pages 471-475, 22 references, 1996.
A study was conducted examining variations in styrene (100425) metabolism over the course of a workweek in styrene exposed workers as well as the effects of acetone (67641) exposure on styrene metabolism. Styrene and acetone exposure were monitored in 44

fiberglass workers on Monday and Thursday of the same workweek using passive dosimeters. In addition, urinary levels of mandelic-acid (MA) and phenylglyoxylic-acid (PGA) were determined at the end of the work shifts on Monday and Thursday and before the start of the work shifts on Tuesday and Friday. The mean 8 hour time weighted average (TWA) styrene and acetone exposure values were 187.9 and 308mg/m3, respectively, on Monday and 203.8 and 256.4mg/m3, respectively, on Thursday. These values were not significantly different between days. The Threshold Limit Values (TLV) recommended by the American Conference of Governmental Hygienists (ACGIH) for styrene was exceeded for 26 workers on Monday and for 20 workers on Thursday. No acetone measurements were in excess of ACGIH TLV/TWA recommended levels. ACGIH recommended biological exposure indices for MA and PGA were exceeded in many workers both at the end of the work shift and the next morning. Urinary excretion of MA and PGA at the end of a workshift was significantly higher on Thursday compared with Monday and MA and PGA excretion were significantly higher on Friday compared with Monday before the workshift. The excretion of MA and PGA was found to correlate with styrene, but not acetone, exposure. The authors conclude that variations in the excretion of MA and PGA over the course of a work week should be taken into account when establishing biological exposure limits.

Code(s): 11.
Mlynarek, S., M. Corn and C. Blake. (1996). "Asbestos exposure of building maintenance personnel." Regul Toxicol Pharmacol. 23 (3): 213-24.
The exposures of building maintenance personnel and occupants to airborne asbestos fibers, and the effects of operations and maintenance programs on those exposures, continue to be an important public health issue. The subject of this investigation was a large metropolitan county with numerous public buildings which routinely conducted air sampling for asbestos. A total of 302 personal air samples in nine task categories collected during maintenance worker activities in proximity to asbestos-containing materials were analyzed; 102 environmental air samples in four task categories were also analyzed. The arithmetic means of the 8-hr time weighted average exposures for personal sampling for each task category were all below the Occupational Safety and Health Administration permissible exposure level of 0.1 fibers (f)/cc > 5 microm. The highest mean 8-hr time weighted average exposure was 0.030 f/cc > 5 microm for ceiling tile replacement. The maximum asbestos concentration during sample collection for environmental samples was 0.027 f/cc > 5 microm. All asbestos-related maintenance work was done within the framework of an Operations and Maintenance Program (OMP) which utilized both personal protective equipment and controls against fiber release/dispersion. Results are presented in association with specific OMP procedures or controls. These results support the effectiveness of using Operations and Maintenance Programs to manage asbestos in buildings without incurring unacceptable risk to maintenance workers performing maintenance tasks.

Code(s): 11.
Quinn, M. M., T. J. Smith, M. J. Ellenbecker, D. H. Wegman and E. A. Eisen. (1996). "Biologically Based Indices of Exposure to Fibres for Use in Epidemiology." Occupational Hygiene, Vol. 3, Nos. 1-3, pages 103-111, 19 references, 1996 AB - A biologically based index of exposure to airborne fibers for use in an epidemiological study of lung cancer in workers producing man made vitreous fibers (MMVF) was presented. The approach was designed to take alternative hypotheses into account by identifying different fiber subsets, particularly those with relevance for lung cancer. The subsets were designated "hypothetically active fibers" (HAF) indices and were based on three criteria for biological activity: the ability to induce cellular changes characteristic of tumor formation; the expectation that they would reach the target tissue; and that they would persist in that tissue long enough to produce carcinogenic cellular changes. Four matrices were constructed, with one representing an airborne fiber count by length and diameter for a particular exposure setting and three representing each of the three HAF criteria. Values in the matrix cells represented specific hypotheses for defining each condition, which can be changed depending on the hypothesis to be examined. Hypotheses about the roles of fiber composition and dimensions in meeting the three HAF conditions were used to construct the index HAF1. Matrices were constructed through linked spreadsheets using a personal computer and the fiber number matrix was multiplied by the three biological criteria matrices to produce the index. Fiber subsets identified as HAF1 differed from those identified with previously published exposure indices. HAF indices did not necessarily correlate with indices previously used in epidemiology studies. The authors conclude that exposure/response relationships can be obscured by exposure measures that do not represent biologically active exposure.

Code(s): 11.
Schneider, T., G. Burdett, L. Martinon, P. Brochard, M. Guillemin, U. Teichert and U. Draeger. (1996). "Ubiquitous fiber exposure in selected sampling sites in Europe." Scand J Work Environ Health. 22 (4): 274-84.
OBJECTIVES: This study evaluates personal exposure to respirable inorganic and organic fibers during normal human lifetimes and assesses the order of magnitude of the contribution of inorganic fibers other than asbestos to total fiber exposure from man-made and natural sources. METHODS: Four groups (suburban schoolchildren, rural retired persons, office workers, and taxi drivers), with five persons per group, were monitored for 24 h four times during one year. Personal sampling pumps collected airborne dust on gold-precoated Nuclepore filters. The fibers were analyzed for fiber sizes specified by the World Health Organization. RESULTS: The geometric mean concentrations ranged from 9000 fibers.m-3 (office workers) to 20000 fibers.m-3 (schoolchildren) for organic fibers, and from 600 fibers.m-3 (taxi drivers) to 4000 fibers.m-3 (schoolchildren) for gypsum fibers. For other inorganic fibers the

concentrations were around 5000 fibers.m-3. The contribution of fibers with an elemental composition similar to that of man-made vitreous fibers (MMVF) was less than about one-quarter of the content of other inorganic fibers. The fiber size distributions were uniform across the groups, and the organic fibers were the longest and thinnest nonasbestos fibers. CONCLUSIONS: Lifetime exposure to fibers can be ranked as organic fibers > other inorganic fibers > fibers with an elemental composition similar to MMVF > MMVF. Information on the biological effects of fibers is difficult to interpret for use in assessing the health risk from exposure to low levels of ubiquitous fibers, and there is a lack of knowledge on the effects of organic fibers.

Code(s): 11.
Stone, R. A., G. M. Marsh, A. O. Youk, T. J. Smith and M. M. Quinn. (1996). "Statistical Estimation of Exposure to Fibres in Jobs for which no Direct Measurements are Available." Occupational Hygiene, Vol. 3, Nos. 1-3, pages 91-101, 8 references, 1996.
Some statistical aspects of the modeling of exposure that provide estimated exposures to fibers to be used as predictor variables in the analysis of mortality were considered. Specifically, the statistical properties of estimates of exposure, for jobs with no direct measurements, that are constructed as weighted averages of measured exposure were described. A formula for the variance of such weighted averages that allows for uncertainty was derived. Preliminary data on exposure from a fibrous glass factory was used to illustrate the statistical methods. The weights were estimated proportions of the time workers spent in areas of potential exposure for which measurements were available. Preliminary fiber concentration data from the current United States cohort, of workers exposed to man made vitreous fibers, were used to demonstrate the method. Mortality data among 30,000 workers, employed in six rockwool and 14 fibrous glass factories, between 1945 and 1986, for at least 1 year, were used. The retrospective exposure assessment was based on work history information contained in company personnel records and included job analysis, technical history analysis and analysis of airborne fiber data. Man made vitreous fiber exposure estimates that were work area and time specific for total and respirable fibers, were examined. Underestimation of variability in estimated exposures based on weighted averages, can occur if uncertainty in the weights is not taken into account. Weighted averages of disparate exposures can be affected by estimated job component fraction values. The derived formula for variance in weighted averages, allows for the uncertainty in weights. The authors state that the inherent uncertainty in exposure modeling, along with between and within worker variability, contributes to variability in estimated exposures used in mortality predictions. They conclude that several sources of exposure modeling uncertainty can be identified and quantified.

Code(s): 11.
Thriene, B., A. Sobottka, H. Willer and J. Weidhase. (1996). "Man-Made Mineral Fibre Boards in Buildings Health Risks Caused by Quality Deficiencies." Toxicology Letters, Vol. 88, Nos. 1-3, pages 299-303, 1 reference, 1996.
Measurements of sources and types of pollutants were made to address complaints of allergic symptoms in workers in a modern office building. The air inside the rooms on all four floors was monitored, followed by scanning electron microscopy of inorganic fibrous particles. The 133 workers were questioned about health problems. A total of 79 workers complained about itching, redness, and burning eyes, tears, hay fever, and upper respiratory tract irritations. False ceilings were loosely installed in a ceiling system in all rooms. The edges were unsealed and partly frayed. An unusually high degree of dust accumulated on furniture and equipment. A relationship was found between the amount of fiber dust accumulation in the office and the number of health complaints by the employees. The fibers in the dust were identical with those used in the man made mineral fiber ceiling boards. Mineral fiber composition levels were measured between 1,000 to 3,500/cubic meter. The ceiling boards likely did not meet standard specifications. Unsatisfactory paint coating was the primary reason for fiber release. The authors conclude that the offices should be undergo an urgent remediation with regard to the quality of the fiber boards installed.

Code(s): 11.
Wozniak, H. and E. Wiecek. (1996). "[Refractory ceramic fibers, kinds, health effects after exposure, TLVs]." Med Pr. 47 (4): 393-9.
Ceramic fibres are amorphous or crystalline synthetic mineral fibres which are characterised by refractory properties (i.c. stability in temperature above 1000 degrees C). In general, ceramic fibres are produced from aluminium oxide, silicon oxide and other metal oxides and less frequently from non-oxide materials such as silicon carbide, silicon nitride and boron nitride. In Poland, the production of ceramic fibres was begun in the Refractory Materials Plant, Skawina, during mid- eighties. The production capacity accounts for about 600 tons annually. It is estimated that approximately 3000 persons are exposed to the effect of ceramic fibres in Poland. During the production of ceramic fibres, concentrations of respiral fibres in the air at work places range from 0.07 to 0.27 f/cm3; during the manufacture of ceramic fibre products from 0.23 to 0.71 f/cm3 and during the application of ceramic fibre products from 0.07 to 1.67 f/cm3. As published data depict, fibres longer than 5 microns are most common in the work environment, and the proportion of fibres with diameters below 1 micron accounts for 40-50%. Bearing in mind the present situation in Poland, namely combined exposure to asbestos (during removal of worn out heat- insulating materials) and ceramic fibres (during installation of new insulation), as well as in view of own investigations and literature data which evidence a strong carcinogenic effect of certain fibres, the following MAC values have been adopted: Dusts of refractory ceramic fibres: total dust-2 mg/m3; respirable fibres-1 f/cm3 (L > 5 microns; D < 3 microns; L: D < 3:1) Dusts of reflactory ceramic fibres mixed with asbestos: total dust-1 mg/m3; respirable fibres-1 f/m3. Dusts of refractory ceramic fibres mixed with other man-made mineral fibres (MMMF): total dust-2 mg/m3; respirable fibres-1 f/m3. According to the

IARC, ceramic fibres have been included into group 2B-suspected human carcinogen.

Code(s): 11.
Davis, D. R. (1995). "Release of asbestos fibers during casting ring liner manipulation." J Prosthet Dent. 74 (3): 294-8.
Civil lawsuits have been filed that allege wrongful deaths of at least one dentist and one dental technician from asbestos exposure. However, no known published scientific studies support such allegations. To assess what potential exposure could occur, air samples were collected while casting rings were lined with asbestos liner. Fibers were collected on filters and counted by use of phase-contrast microscopy and transmission electron microscopy. The concentrations of fibers 5 microns long or greater on all filters was less than allowed by federal guidelines. Based on this simulation the potential health risk from using asbestos ring liner seems low.

Code(s): 11.
Plato, N., S. Krantz, L. Andersson, P. Gustavsson and L. Lundgren. (1995). "Characterization of current exposure to man-made vitreous fibres (MMVF) in the prefabricated house industry in Sweden." Annals of Occupational Hygiene; 39 (2). 1995. 167-179.
BIOSIS COPYRIGHT: BIOL ABS. The exposure to man-made vitreous fibres (MMVF) was investigated at 11 Swedish plants manufacturing prefabricated wooden houses. Current fibre levels were studied by monitoring personal exposure using the membrane filter technique. All samples were analysed by phase contrast optical microscopy (PCOM) according to Swedish standard rules; they were also analysed using a set of modified criteria for fibre counting, developed for this study, which in addition also required straight, parallel and/or convergent edges of the fibres. The objective of this alternating counting method, the modified fibre method, was to exclude fibres with appearance other than MMVF, that might be present in the wood industries. The method was validated by scanning electron microscopy (SEM). In all, 120 samples were taken and 273 analyses were performed. The mean exposure (GM), analysed by the standard method, was for insulators 0.10 f ml-1 (range 0.03-0.30 f ml-1) and for woodcutters 0.09 f ml-1

Code(s): 11.
Plato, N., S. Krantz, P. Gustavsson, T. J. Smith and P. Westerholm. (1995). "Fiber exposure assessment in the Swedish rock wool and slag wool production industry in 1938-1990." Scand J Work Environ Health. 21 (5): 345-52.
OBJECTIVE--A multiplicative model was developed to assess past exposure to respirable fibers among rock wool and slag wool production workers in Sweden in 1938-1990. METHODS--Information on the job titles, work tasks and employment times of 1487 workers exposed to man-made vitreous fibers was obtained from company records and interviews with older employees. A mathematical model developed earlier for assessing historical fiber exposure, based on factory averages, was further developed. Matrices of multipliers for each plant that were specific for job title were modified to assess fiber exposure with respect to job title and calendar period. The model was based on measurements made in 1977. Two methods of exposure assessment were compared, cumulative exposure based on factory average (model I) and cumulative exposure based on job title (model II). RESULTS--The exposure changed considerably in the two factories during the period 1938-1990, and it varied also between job titles. The estimated average fiber (f) exposure level at the two plants in the middle of the 1940s was 1.32 and 0.78 f.ml-1. These values are 26 and 16 times higher, respectively, than the exposure in 1980. Process changes, as well as the addition of binders and oil, reduced the exposure drastically around 1950. The mean cumulative respirable fiber exposure for the 1487 subjects was 1.44 (range 0.05-18.40) f.ml-1.year. The cleaners had 14 times higher annual fiber exposure than the preproduction workers. CONCLUSIONS--Model II was judged to be more valid than model I in assessing exposure to man- made vitreous fibers.

Code(s): 11.
Schneider, T. (1995). "Physical Characterization of MMVF for Risk Assessment." Annals of Occupational Hygiene, Vol. 39, No. 5, pages 673-689, 21 references, 1995.
Methods used to assess the health risks associated with exposure to man made vitreous fibers (MMVF) were described. Physical characteristics of the fibers themselves should play an important role in the risk assessment. The physical characteristics included fiber diameter, length, number, and specific surface. Durability may be a factor where soluble fibers may change size as they dissolve. Methods for a-priori assessment of exposure were classified into three categories: direct analysis of the fibrous bulk material, bench scale testing, and full scale testing of prefabricated insulation material in a test room during standardized insulation work, considered the gold standard. If only bulk material properties are used to estimate exposure potential, one of two approaches may be used. The first relates size dependent measures to mass of fibers, and spans two to four orders of magnitude. This method distinguishes between different bulk MMVFs. The other considers fractions of total fiber length, spans up to two orders of magnitude, and does not distinguish as successfully the different bulk MMVFs. Bench scale testing included the rotating drum method (for dry powders), vibration tests, shaking tests, and dust release during a tear strength test. The full scale test represented a worst case scenario in that the task consists of cutting and insulating all walls and ceiling, while fiber concentration was monitored with personal samplers. The author reports that the slope of the curve relating overall product nominal diameter and airborne fiber concentration on a log scale has been confirmed on a qualitative basis using model calculations and may be used as a first estimate of changes in exposure due to changes in nominal diameter of bulk material.

Review Papers (14, 15)

Code(s): 14.
(1995). "Toxicological profile for asbestos: Update." U.S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, Division of Toxicology, Toxicology Information Branch, 1600 Clifton Road NE, E-29, Atlanta, GA 30333, USA, Aug. 1995. 192p. Illus. Bibl.ref.
Contents: public health statement; health effects; chemical and physical information; production, import, use and disposal; potential for human exposure; analytical methods; regulations and advisories; glossary. Health hazards include: asbestosis; pleural thickening; lung cancer; pleural mesothelioma; peritoneal mesothelioma; carcinogenic effects. (Update of CIS 91-1259).

Code(s): 14.
Anonymous. (1995). "Toxicological Profile for Asbestos (Update)." Agency for Toxic Substances and Disease Registry, U.S. Department of Health and Human Services, Atlanta, Georgia, 205 pages, 1,134 references, 1995.
This profile on asbestos (1332214) provided information on toxicologic and adverse health effects. The public health statement explained what asbestos is, what happens to asbestos once it enters the environment, how individuals may be exposed to asbestos, how the substance enters and leaves the human body, what effects it can have on health, medical tests to determine whether exposure to asbestos has occurred, recommendations from the federal government to protect human health, and additional sources of information which are listed for people to consider. The section on health effects considered consequences of inhalation exposure, oral exposure, and dermal exposure and in each case considered the potential for death, systemic effects, immunological and lymphoreticular effects, neurological effects, reproductive effects, developmental effects, genotoxic effects, and cancer. Toxicokinetics was reviewed with sections relating to absorption, distribution, metabolism, excretion, and the mechanisms of action. Others topics covered included biomarkers of exposure and effect, interactions with other substances, populations that are unusually susceptible, methods for reducing the toxic effects, adequacy of the database, chemical and physical information, production, importing, use, disposal, potential for human exposure, and analytical methods. Regulations and advisories dealing with asbestos exposure were included.

Code(s): 14.
Brown, M., W. D. Henriques and P. M. Bittner. (1995). "Toxicological Profile for Asbestos (Update, August 1995)." Govt Reports Announcements & Index (GRA&I), Issue 02, 1996.
TD3: This statement was prepared to give you information about asbestos and to emphasize the human health effects that may result from exposure to it. The Enviornmental Protection Agency (EPA) has identified 1,408 hazardous waste sites as the most serious in the nation. Asbestos has been found in at least 58 of the sites on the NPL. See also PB91-180497. Sponsored by Agency for Toxic Substances and Disease Registry, Atlanta, GA. Div. of Toxicology.

Code(s): 14, 15.
Borm, P. J. (2002). "Particle toxicology: from coal mining to nanotechnology." Inhal Toxicol. 14 (3): 311-24.
Particle research has been historically closely connected to industrial activities or materials, such as coal, asbestos, man-made mineral fibers, and more recently ambient particulate matter (PM). It is the purpose of this review to combine insights and developments in particle toxicology with the historical context of exposure and organizations sponsoring such research in Europe. In supporting research on particle- induced respiratory effects and mechanisms, research programs of the European Community on Steel and Coal (ECSC) have played a tremendous role. Current particle research in Europe is dominated by PM, and funded by the World Health Organization (WHO), European Union Framework programs, and the Health Effects Institute (HEI). Differences between historical and current research in particle toxicology include the exposure concentrations, particle size, target populations, endpoints, and length of exposure. Inhaled particle effects are no longer confined to the lung, since particles are suggested to translocate to the blood while lung inflammation invokes systemic responses. Finally, the particle size and concentrations have both been reduced about 100-fold from 2-5 mg/m3 to 20-50 mg/m3 and from 1-2 microm to 20-100 nm (ultrafine) as domestic fuel burning has decreased and vehicle sources have increased and attention has moved from coal mining industry to general environment. There is, however, a further occupational link to nanotechnology, which continuously produces new materials in the ultrafine range. Although inhalation exposure is considered to be minimal in this technology, some particles are produced to be used for carrier purpose in medical applications. Based on our current knowledge of particle toxicology, it is highly desirable that toxicology and technology are linked in this extremely rapid developing area, to learn more about potential risks and also to develop knowledge on the role of surface and size in particle toxicity.

Code(s): 14, 15.
Fubini, B. (1997). "Surface reactivity in the pathogenic response to particulates." Environ Health Perspect. 105 Suppl 5 1013-20.
The peculiar characteristics of dust toxicity are discussed in relation to the processes taking place at the particle-biological medium interface. Because of surface reactivity, toxicity of solids is not merely predictable from chemical composition and molecular structure,

as with water soluble compounds. With particles having the same bulk composition, micromorphology (the thermal and mechanical history of dust and adsorption from the environment) determines the kind and abundance of active surface sites, thus modulating reactivity toward cells and tissues. The quantitative evaluation of doses is discussed in comparisons of dose-response relationships obtained with different materials. Responses related to the surface of the particle are better compared on a per-unit surface than per-unit weight basis. The role of micromorphology, hydrophilicity, and reactive surface cations in determining the pathogenicity of inhaled particles is described with reference to silica and asbestos toxicity. Heating crystalline silica decreases hydrophilicity, with consequent modifications in membranolytic potential, retention, and transport. Transition metal ions exposed at the surface generate free radicals in aqueous suspensions. Continuous redox cycling of iron, with consequent activation-reactivation of the surface sites releasing free radicals, could account for the long-term pathogenicity caused by the inhalation of iron-containing fibers. In various pathogenicities caused by mixed dusts, the contact between components modifies toxicity. Hard metal lung disease is caused by exposure to mixtures of metals and carbides, typically cobalt (Co) and tungsten carbide (WC), but not to single components. Toxicity stems from reactive oxygen species generation in a mechanism involving both Co metal and WC in mutual contact. A relationship between the extent of water adsorption and biopersistence is proposed for vitreous fibers. Modifications of the surface taking place in vivo are described for ferruginous bodies and for the progressive comminution of chrysotile asbestos fibers.

Code(s): 15.
Hesterberg, T. W., G. A. Hart and W. B. Bunn. (1993). "In Vitro Toxicology of Fibers: Mechanistic Studies and Possible Use for Screening Assays." Fiber Toxicology, D. B. Warheit, Editor; Academic Press, Inc., San Diego, pages 139-170, 102 references, 1993.
The published literature on the in-vitro toxicology of man made vitreous fibers (MMVF) and other man made inorganic and organic fibers was reviewed, and determinations were made of test fiber compositions and in-vitro systems with the greatest potential for use in toxicity assays. The working model of the mechanisms of fiber pathogenicity was described, including fiber associated diseases induced by asbestos (1332214) and MMVF exposure, and the immunological reactions involved with inflammation/fibrogenesis and oncogenesis. In-vitro studies of fiber toxicology can be grouped in the three categories of cytotoxicity studies, inflammation and fibrogenesis model studies, and genotoxicity studies. Studies of cytotoxicity were cited for fibrous glass, mineral wood, ceramic fibers, aramid fibers, carbon fibers, and polyolefins. General considerations for cytotoxicity studies included comparisons between fibers of similar lengths and diameters, chemistry, crystallinity, surface area, mean and median dimensions, accurate expressions of fiber exposure, and methodology. Studies that model inflammation and fibrogenesis were cited for fibrous glass, chrysotile (12001295), quartz (14808607), crocidolite (12001284), amosite (12172735), anthophyllite (7631869), wollastonite (13983170), carbonyl-iron (7439896) particles, zymosan (9010724), silica, latex beads, and asbestos, with emphasis on the role of macrophages and other phagocytic cells in the development of lung disease. Studies of genotoxicity were mentioned for the occurrences of transformation, aneuploidy and polyploidy, clastogenesis, gene mutagenesis, transfection, and oncogene activation induced in various in-vitro systems from exposure to fibers. The authors conclude that in-vitro studies can serve as a substantial aid in short term fiber toxicity screening, although it is necessary to compare the in-vitro toxic effects of sized and well characterized fibers with pathogenesis in long term animal studies.

Unknown Relevance (90)

Code(s): 90.
Lioy, P. J., C. P. Weisel, J. R. Millette, S. Eisenreich, D. Vallero, J. Offenberg, B. Buckley, B. Turpin, M. Zhong, M. D. Cohen, C. Prophete, I. Yang, R. Stiles, G. Chee, W. Johnson, R. Porcja, S. Alimokhtari, R. C. Hale, C. Weschler and L. C. Chen. (2002). "Characterization of the dust/smoke aerosol that settled east of the World Trade Center (WTC) in lower Manhattan after the collapse of the WTC 11 September 2001." Environ Health Perspect. 110 (7): 703-14.
The explosion and collapse of the World Trade Center (WTC) was a catastrophic event that produced an aerosol plume impacting many workers, residents, and commuters during the first few days after 11 September 2001. Three bulk samples of the total settled dust and smoke were collected at weather-protected locations east of the WTC on 16 and 17 September 2001; these samples are representative of the generated material that settled immediately after the explosion and fire and the concurrent collapse of the two structures. We analyzed each sample, not differentiated by particle size, for inorganic and organic composition. In the inorganic analyses, we identified metals, radionuclides, ionic species, asbestos, and inorganic species. In the organic analyses, we identified polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls, polychlorinated dibenzodioxins, polychlorinated dibenzofurans, pesticides, phthalate esters, brominated diphenyl ethers, and other hydrocarbons. Each sample had a basic pH. Asbestos levels ranged from 0.8% to 3.0% of the mass, the PAHs were > 0.1% of the mass, and lead ranged from 101 to 625 microg/g. The content and distribution of material was indicative of a complex mixture of building debris and combustion products in the resulting plume. These three samples were composed primarily of construction materials, soot, paint (leaded and unleaded), and glass fibers (mineral wool and fiberglass). Levels of hydrocarbons indicated unburned or partially burned jet fuel, plastic, cellulose, and other materials that were ignited by the fire. In morphologic analyses we found that a majority of the mass was fibrous and composed of many types of fibers (e.g., mineral wool, fiberglass, asbestos, wood, paper, and cotton). The particles were separated into size classifications by gravimetric

and aerodynamic methods. Material < 2.5 microm in aerodynamic diameter was 0.88-1.98% of the total mass. The largest mass concentrations were > 53 microm in diameter. The results obtained from these samples can be used to understand the contact and types of exposures to this unprecedented complex mixture experienced by the surviving residents, commuters, and rescue workers directly affected by the plume from 11 to 12 September and the evaluations of any acute or long-term health effects from resuspendable dust and smoke to the residents, commuters, and local workers, as well as from the materials released after 11 September until the fires were extinguished. Further, these results support the need to have the interior of residences, buildings, and their respective HVAC systems professionally cleaned to reduce long-term residential risks before rehabitation.

Code(s): 90.
Marchant, G. E., M. A. Amen, C. H. Bullock, C. M. Carter, K. A. Johnson, J. W. Reynolds, F. R. Connelly and A. E. Crane. (2002). "A synthetic vitreous fiber (SVF) occupational exposure database: implementing the SVF Health and Safety Partnership Program." Appl Occup Environ Hyg. 17 (4): 276-85.
The Health and Safety Partnership Program is a voluntary workplace safety program for workers involved in the manufacture, fabrication, installation, and removal of glass wool and mineral wool products. This article describes one element of this Partnership Program, the development of an occupational exposure database that characterizes exposures by fiber type, industry sector, product type, and job description. Approximately 6000 exposure samples are included in the database, most of which were collected over the past decade, making it the most extensive and recent exposure data set on record for glass wool and mineral wool. The development of this database, as well as the initial results for exposure measurements segmented by product type and/or job description, are described. The current database shows that most applications and uses of glass wool and mineral wool involve exposures below the voluntary 1 f/cc permissible exposure limit, although some specific product types and job descriptions involve average exposures approaching the 1 f/cc limit.

Code(s): 90.
Lange, J. H. and K. W. Thomulka. (2000). "Air sampling during asbestos abatement of floor tile and mastic." Bull Environ Contam Toxicol. 64 (4): 497-501.

Code(s): 90.
Alessio, L., G. Chiappino, V. Foα, S. Basilico, L. Riboldi, G. Rivolta, M. Barducci, G. Errigo, O. Picchi, D. Consonni, I. Bernucci, P. A. Bertazzi and G. A. Aresini. (1999). "Environmental and occupational exposure to vitreous fibres." Medicina del lavoro Jan.-Feb. 1999, Vol.90, No.1, p.3-89. (whole issue). Illus. 161 ref.
Topics: carcinogenic effects; ceramic fibres; classification; conference; exposure; glass fibre; health hazards; legal aspects; lung cancer; man-made fibres; mineral wool; pulmonary fibrosis; respirable dust; respiratory diseases; toxicology.

Code(s): 90.
Marsh, G. M., R. A. Stone, A. O. Youk and T. J. Smith. (1998). "Cancer mortality among man-made vitreous fiber production workers." Epidemiology. 9 (2): 218; discussion 214-20.

Code(s): 90.
Oliver, L. C. (1998). "Asbestos in Buildings Management and Related Health Effects." Journal of Clean Technology Environmental Toxicology and Occupational Medicine; 7 (4). 1998. 433-443.
Biosis copyright: biol abs. rrm literature review human occupational health toxicology asbestos buildings exposure occupational exposure carcinogen toxin management related health effects asbestos-containing material

Code(s): 90.
Boffetta, P. (1997). "Mortality of Man-Made Vitreous Fibre Workers in Europe." Eighty-Eighth Annual Meeting of the American Association for Cancer Research, San Diego, California, USA, April 12-16, 1997. Proceedings of the American Association for Cancer Research Annual Meeting; 38 (0). 1997. 298-299.
Biosis copyright: biol abs. rrm meeting abstract human man-made vitreous fiber worker rock-slag wool worker patient glass wool worker oncology epidemiology statistical analysis mortality man-made vitreous fiber workers occupational health lung cancer asbestos carcinogens 1950-1990 toxicity respiratory system disease neoplastic disease europe palearctic region

Code(s): 90.
Gold, J., H. Amandusson, A. Krozer, B. Kasemo, T. Ericsson, G. Zanetti and B. Fubini. (1997). "Chemical Characterization and Reactivity of Iron Chelator-Treated Amphibole Asbestos." Environmental Health Perspectives, Vol. 105, Supplement 5, pages 1021-1030, 42 references, 1997.
The effects of iron chelator treatments on the characterization and reactivity of crocidolite (12001284) and amosite (12172735) fibers

were examined. The fibers were incubated with 10 millimolar solutions of desferrioxamine, sodium-ascorbate, ferrozine, or phosphate buffer for 3 days. Following incubation, the iron (7439896) content of the fibers was determined using atomic absorption spectroscopy and inductively coupled plasma atomic emission spectroscopy. The bulk iron and surface iron of dried fibers were characterized using Mossbauer spectroscopy and X-ray photoelectron spectroscopy, respectively. Electron paramagnetic resonance spectroscopy was applied to the measurement of free radical generation in aqueous fiber suspensions. An enzymatic assay was used to determine hydrogen-peroxide (H2O2) decomposition in the fibers. Chelator treatment removed 1 to 5% of the total iron content from the crocidolite and amosite fibers. The phosphate buffer solution caused the least amount of iron mobilization. Generally, iron mobilization was greater with crocidolite fibers than with amosite fibers. Based on bulk iron analysis, amosite contained only ferric ions, while crocidolite was composed of both ferrous and ferric ions. Bulk ion content was not affected by chelator treatment. Surface iron concentrations were reduced significantly by desferrioxamine and sodium-ascorbate in crocidolite fibers and desferrioxamine, ferrozine, and phosphate-buffer in amosite fibers. For both fiber types, surface iron was primarily in the ferric state. The proportion of ferrous iron on the surface of amosite fibers increased with chelator treatment. Desferrioxamine treatment increased the surface content of nitrogen. The release of carboxylate free radicals was reduced by chelator treatment, especially in amosite fibers. Phosphate buffer stimulated the generation of hydroxyl radicals in amosite and crocidolite fibers. The H2O2 catalytic activity of both fiber types was decreased following chelator treatment. The authors conclude that iron chelators alter the surface iron and iron mobilization characteristics of crocidolite and amosite fibers.

Code(s): 90.
Lemen, R. A. (1997). "Introduction: history of the use of asbestos." Med Lav. 88 (4): 288-92.
Discussion of the major milestones in the history of the modern uses of asbestos and the first knowledge of the health effects associated with such usage. Highlights of the studies associating exposure to asbestos with non-malignant lung diseases, lung cancer, and mesothelioma are discussed.

Code(s): 90.
Merler, E. (1997). "[The INSERM report "The effects on health of the main asbestos exposures" and the decision to ban asbestos in France]." Epidemiol Prev. 21 (1): 10-3.

Code(s): 90.
McConnell, E. E. (1995). "Advantages and limits of in vivo screening tests." Ann Occup Hyg. 39 (5): 727-35.
Several methods have been proposed to ascertain the potential toxicity of man-made vitreous fibres (MMVF) in animals. The most frequently used in vivo methods include inhalation (IH) (whole body and nose-only), intratracheal (IT) instillation, intrapleural injection-implantation and intraperitoneal (IP) injection. This report compares reports of studies using these methods in terms of their: (1) relevance to humans; (2) standardization of technique; (3) validation of method; (4) need for fibre preparation; (5) estimation of maximum tolerated dose; (6) determination of 'overload'; (7) exposure regimen; (8) pathology requirements; (9) quality control procedures; (10) extent and type of peer review; and (11) value of data for risk assessment. The results of this investigation showed that the inhalation method was clearly superior to the other exposure methods in all respects, although it is the most expensive. The intratracheal instillation method was considered a second choice, while injection-implantation methods were fraught with scientific and practical problems and the data derived from studies using these techniques were considered of value only for the study of specific mechanistic issues.

Code(s): 90.
Mueller, B. (1995). "Effects of Environmental Factors on the Lung Surfactant System." Seminars in Respiratory and Critical Care Medicine; 16 (1). 1995. 53-60.
Biosis copyright: biol abs. rrm literature review human rat silica asbestos ozone nitrogen dioxide toxicity

Code(s): 90.
Rao Mohan, N. and P. K. Kulkarni. (1995). "Pulmonary Function Evaluation in Subjects Occupationally Exposed to Toxic Dust and Pollutants." Indian Journal of Industrial Medicine; 41 (4). 1995. 162-166.
Biosis copyright: biol abs. rrm research article human occupational health biobusiness occupational health and safety pulmonary function evaluation toxic dust-pollutants toxicity toxicology pollution smoking cotton dust asbestos dust occupational exposure

Code(s): 90.
Upton, A. C. and R. A. Shaikh. (1995). "Asbestos exposures in public and commercial buildings." Am J Ind Med. 27 (3): 433-7; discussion 439-41.

Suggested "Charge" Publications

1. Code(s): 1, 2.
Wrzaszczyk, B. and H. Owczarek. (1996). "Relationship between the physiochemical properties of asbestos and pulmonary fibrosis." Med Pr. 47 (4): 401-9.
The work presents a review of the literature on the effect of physiochemical properties on the intensity of pulmonary fibrosis. Exposure to asbestos fibres induces inflammatory processes which contribute to collagen deposition in the lung tissue. The toxicity of asbestos fibres depends on physiochemical properties of asbestos. Owing to their advantageous aerodynamics, straight needle-like amphiboles can penetrate much easier into the pulmonary tissue than curly serpentine fibres. With magnesium as its main cation, chrysotile has an unstable structure and tends towards the fragmentation into smaller particles. Therefore, its phagocytosis by macrophages and its clearance from the lung tissue are more effective than those of amphiboles. On the other hand, chrysotile undergoes longitudinal fragmentation into thin elementary particles, thus, it proliferates easier respirable fibres in the pulmonary tissue. Fibrosis induced by long fibres (L < 5 microns) is more extensive than that produced by short fibres (L < 5 microns) because of incomplete phagocytosis by macrophages which releases a stimulus to the synthesis of fibronectin and collagen.

2. Code(s): 1, 2, 8.
Hart, G. A., L. M. Kathman and T. W. Hesterberg. (1994). "In vitro cytotoxicity of asbestos and man-made vitreous fibers: roles of fiber length, diameter and composition." Carcinogenesis. 15 (5): 971-7.
The present study investigated (i) the impact of various fiber parameters on in vitro toxicity to cells and (ii) the validity of an in vitro test system as a toxic screen for fibrous materials. Chinese hamster ovary cells were exposed in vitro to a series of size-selected inorganic test fibers that represented a range of different diameters, lengths and compositions (glass, refractory ceramic, mineral wool, asbestos). Toxic end-points included inhibition of proliferation, induction of micronuclei and polynuclei and viability. For all compositions tested, toxic effects were similar: a concentration- dependent decrease in proliferation and increase in incidence of morphologically abnormal nuclei with minor decreases in viability. Diameter-dependent differences in toxicity were slight or absent for fiber diameters ranging from 0.3-7 microns when concentration was expressed as number of fibers/cm2. Length-dependent differences in toxicity were, however, striking. EC50 values (concentration in fibers/cm2 that reduced cell proliferation to 50% of unexposed control cultures) plotted against fiber length produced a hyperbolic curve, demonstrating that toxicity increases with fiber length up to 20 microns. All fibers tested fell on this hyperbola. These data suggest that: (a) the primary toxic effect of fibers on CHO cells is the induction of nuclear morphologic alterations resulting in cytostasis; (b) fiber diameter has little or no impact on in vitro toxicity when concentration is calculated as fibers/cm2; (c) fiber length is directly proportional to in vitro toxicity; and (d) toxicity of asbestos and vitreous fibers to CHO cells is not affected by composition. The lack of compositional effect in CHO cells does not correlate with findings from recent rodent inhalation studies using the same test fibers. Thus CHO cells may not be an appropriate in vitro model of fiber pathogenesis and would not constitute a valid toxicologic screening system for fibers.

3. Code(s): 2, 5, 7, 8, 9, 15.
Foa, V. and S. Basilico. (1999). "Chemical and physical characteristics and toxicology of man-made mineral fibers." Med Lav. 90 (1): 10-52.
The evidence for the adverse health effects following exposure to asbestos (i.e. fibrogenic and carcinogenic effect) has prompted widespread removal of asbestos-containing materials and led to banning of asbestos internationally (in Italy, DPR 257/1992), resulting in the increased use of substitutes composed of both naturally occurring and synthetic materials, including man made mineral fibres (MMMFs) and man made organic fibres (MMOF). MMMFs represent a family of synthetic, inorganic vitreous substances derived primarily from glass, rock, slag, or clay. MMMFs are further divided into two categories: 1) man made vitreous fibres (MMVFs), further divided as follows: a) fibrous glass, including mainly continuous filament, special purpose fibres; and microfibres. The materials are typically composed of oxides of silicon, calcium, sodium, potassium, aluminum, and boron. b) Mineral wool, including glass wool, rock wool (derived from magma rock) and slag wool (made from molten slag produced in metallurgical processes such as the production of iron, steel, or copper). The main components of rock wool and slag wool are oxides of silicon, calcium, magnesium, aluminum, and iron. 2) Refractory/ceramic fibres, amorphous or partially crystalline materials made from kaolin clay or oxides of aluminum, silicon or other metal oxides (i.e. oxides of zirconium and yttrium). Less commonly, refractory fibres are also made from non-oxide refractory materials such as silicon carbide, silicon nitride, or boron nitride. Industrial production of MMVFs began in the second half of the 19th century, while ceramic fibres production began more recently, in the early 1970s. Major uses of MMMFs include thermal, acoustic and aerospace insulation, fire proofing, reinforcing material in plastics, cement and textile, optic fibres, air and liquid filtration, friction products, refractory coatings. Serious questions have been raised about health implications of MMMFs. Suspicion about the possible occurrence of adverse effects following exposure to MMMFs arises mainly from some similarities of MMMFs with asbestos (fibrous aspects, inhalability, chemical composition, free radical formation). The fibre characteristics that have been identified as crucial in influencing the pathogenesis of fibre-related adverse respiratory effects can be mainly divided into two

groups: fibre dimension, and chemical composition and structure. Fibre dimension plays a determining role in conditioning penetration in the lung. In a broad sense, the term "respirable" means "capable of being carried by breath into the respiratory system". For regulatory purposes, "respirable fibres" (i.e. RFP) are defined in most countries following WHO criteria: length > 5 microns, diameter < 3 microns, length/diameter > 3. MMMFs are generally produced as fibres of diameter higher than asbestos, and too large in diameter to be respirable. Moreover, due to the production process, they are structurally amorphous. Since MMMFs have no crystalline domains, they also have no clearly defined structural faults and they fracture transversely, and randomly. Fragments that are too large to be taken up by macrophages can be resolved in the lung by a leaching--or dissolution--process which leads to a progressive reduction of particle length. In contrast, when abraded, asbestos tends to split longitudinally into new, fine, straight fibres: these fibrils are of much smaller diameter, more respirable, and consequently more hazardous than parent fibres. Fibre chemical composition plays a determining role in conditioning the higher or lower biological activity, durability, biopersistence, and biodegradability. The term "biological activity" means reactivity or ability to interact (possibly due to formation of active oxygen species, identified as a crucial step in the mechanism of action) with biological structures and tissues. Fibre "durability" is strictly related to its solubility. It can be defined as the ability to resist

4. Code(s): 2, 5, 7, 8, 9, 15.
Maxim, L. D. and E. E. McConnell. (2001). "Interspecies comparisons of the toxicity of asbestos and synthetic vitreous fibers: a weight-of-the-evidence approach." Regul Toxicol Pharmacol. 33 (3): 319-42.
This analysis reviews the available literature on interspecies comparisons of the toxicity of asbestos and synthetic vitreous fibers (SVFs). This topic is of substantial practical importance because most quantitative risk analyses on the effects of inhalation of SVFs are based upon extrapolation of data from rodent inhalation studies. Available information on interspecies comparisons for both dosimetry (the relation between exposure concentration and fiber lung burden) and potency (the relation between lung burden and disease) is summarized. Dosimetry models indicate that, on a normalized basis, fiber deposition and clearance rates are lower in humans than rats. Potency is less well understood than dosimetry, in part because the source of relevant human data is asbestos studies, which are adequate to demonstrate hazard, but are problematic in other regards. There are significant interspecies differences between the mouse, hamster, rat, and human. The available evidence suggests that the rat is preferable as a model for the human. Rats develop fibrosis at comparable lung burdens [10(6) long (> 20 microm length) fibers per gram of dry lung] to those in humans. This analysis concludes that, on a weight-of-evidence basis, there is no reason to conclude that humans are more sensitive to fibers than rats with respect to the development of lung cancer.

5. Code(s): 3.
Bridgman, S. A. (2000). "Acute health effects of a fire associated with asbestos-containing fallout." J Public Health Med. 22 (3): 400-5.
BACKGROUND: In September 1994 in a disused leather factory in Tranmere, Wirral, England, there was a fire associated with asbestos-containing fallout in an urban area. This study aimed to describe the acute health effects of this acute environmental incident. METHODS: Descriptive epidemiology of acute health effects of the fire was based on solicitors' letters from compensation claimants, hospital admissions for asthma and other respiratory diseases, accident and emergency records, occupational health records of fire-fighters and police, reports of cases by general practitioners (GPs), and geographical location of calls for help and claimants. RESULTS: Sixteen thousand people lived in the area worst affected by fallout. There were 344 claimants. Eighty-six per cent of claimants had a health complaint, with a total of 728 symptoms or diseases reported to be a consequence of the fire. Seventy per cent of complaints related to the respiratory tract, with 33 per cent of claimants noting sore throat, 31 per cent cough, 9 per cent exacerbated asthma, 8 per cent breathing problems and 13 per cent headaches. The number of hospital admissions for asthma and other lung diseases 1 day, 2 days, 7 days and 28 days after the date of the incident tended to be lower in the year of the fire than in other years. Within 72 h of the fire no cases connected with the fire were seen in the local accident and emergency unit. The geographical location of calls for help to the environmental health department was different from that for compensation claimants. CONCLUSIONS: Hundreds of people sought compensation for the acute health consequences of the fire. Many symptoms or diseases in 344 people were attributed to the fire, but there is no hard evidence to suggest that these were directly due to the fire, although some may have been indirectly attributable to it.

6. Code(s): 3, 6, 8, 9.
Osinubi, O. Y., M. Gochfeld and H. M. Kipen. (2000). "Health effects of asbestos and nonasbestos fibers." Environ Health Perspect. 108 Suppl 4 665-74.
Exposures to asbestos and synthetic fibers remain areas of great concern in the field of occupational lung disease. Despite extensive study, the health effects associated with fibers remains an area of substantial controversy. In particular, effects of fibers at relatively low doses, particularly for mesothelioma, remain a matter of evolving opinion, especially when integrated with the divergence of opinion on relative pathogenicity of different fiber types. Mechanistic studies continue to provide a window into pathogenesis and some hope for understanding dose-response relationships at the lower levels seen in contemporary Western workplaces and the general

environment. Changes in clinical assessment based on use of new chest imaging techniques beyond the traditional plain film are also an area of evolution and begin to challenge B-reading as the definitive tool for noninvasive assessment of disease. Public health concerns have to a great extent been transported to the developing world where there is a strong trend toward increased use of asbestos, although it has been virtually eliminated from commerce in most developed countries. For nonasbestos fibers, the major unsettled issues are their relative potencies as carcinogens for the human lung and mesothelium and the need to sort out the relation between physical and chemical properties of these fibers and their pathogenicity. The recent discovery of "flock worker's lung" due to synthetic fibers once again alerts us to emerging diseases associated with new technologies.

7. Code(s): 3, 7, 8.

Warheit, D. B., G. A. Hart, T. W. Hesterberg, J. J. Collins, W. M. Dyer, G. M. Swaen, V. Castranova, A. I. Soiefer and G. L. Kennedy, Jr. (2001). "Potential pulmonary effects of man-made organic fiber (MMOF) dusts." Crit Rev Toxicol. 31 (6): 697-736.
In the first half of the twentieth century epidemiologic evidence linked elevated incidences of pulmonary fibrosis and cancer with inhalation of chrysotile and crocidolite asbestos, a family of naturally occurring inorganic fibrous materials. As the serpentine and amphibole forms of asbestos were phased out, synthetic vitreous fibers (SVFs; fiber glass, mineral wool, and refractory fiber) became increasingly utilized, and concerns were raised that they too might cause adverse health effects. Extensive toxicological research on SVFs has demonstrated that their pulmonary effects are directly related to fiber dose in the lung over time. This is the result of deposition (thin fibers deposit in the lower lung more efficiently than thick fibers) and lung-persistence ("biopersistence" is directly related to fiber length and inversely related to dissolution and fragmentation rates). In rat inhalation studies, asbestos was determined to be 7- to 10-fold more biopersistent in the lung than SVFs. Other than its effect on biopersistence, fiber composition did not appear to play a direct role in the biological activity of SVFs. Recently, the utilization of man-made organic fibers (MMOFs) (also referred to by some as synthetic organic fibers) has increased rapidly for a variety of applications. In contrast to SVFs, research on the potential pulmonary effects of MMOFs is relatively limited, because traditionally MMOFs were manufactured in diameters too thick to be respirable (inhalable into the lower lung). However, new developments in the MMOF industry have resulted in the production of increasingly fine-diameter fibers for special applications, and certain post-manufacturing processes (e.g., chopping) generate respirable-sized MMOF dust. Until the mid-1990s, there was no consistent evidence of human health affects attributed to occupational exposure to MMOFs. Very recently, however, a unique form of interstitial lung disease has been reported in nylon flock workers in three different plants, and respirable-sized nylon shreds (including fibers) were identified in workplace air samples. Whether nylon dust or other occupational exposures are responsible for the development of lung disease in these workers remains to be determined. It is also unknown whether the biological mechanisms that determine the respirability and toxicity of SVFs apply to MMOFs. Thus, it is appropriate and timely to review the current data regarding MMOF workplace exposure and pulmonary health effects, including the database on epidemiological, exposure assessment, and toxicology studies.

8. Code(s): 6, 9.

Rodelsperger, K., K. H. Jockel, H. Pohlabeln, W. Romer and H. J. Woitowitz. (2001). "Asbestos and man-made vitreous fibers as risk factors for diffuse malignant mesothelioma: results from a German hospital-based case- control study." Am J Ind Med. 39 (3): 262-75.
BACKGROUND: This study examines the role of occupational factors in the development of diffuse malignant mesothelioma with special emphasis on the dose-response relationship for asbestos and on the exposure to man- made vitreous fibers (MMVFs). METHODS: One hundred and twenty-five male cases, diagnosed by a panel of pathologists, were personally interviewed concerning their occupational and smoking history. The same number of population controls (matched for sex, age and region of residence) underwent similar interviews by trained interviewers. Odds ratios (OR) were calculated for an expert-based exposure index using conditional logistic regression. RESULTS: Exposure to asbestos shows the expected sharp gradient with an OR of about 45 for a cumulative exposure > 1.5 fiber years (arithmetic mean 16 fiber years). A significant OR was calculated even for the lowest exposure category "> 0 - < or = 0.15 fiber years". Although the mean cumulative exposure to MMVF is roughly 10% of the exposure to asbestos, an increased OR is observed in an ever/never evaluation. This observation is heavily hampered by methodical problems. A corresponding case-control study was performed using a lung tissue fiber analysis in addition to interviews. Both interviews and the lung tissue analysis yielded similar OR levels between the reference and the maximum exposure intervals. CONCLUSIONS: Despite a possible influence as a result of selection and information bias, our results confirm the previously reported observation of a distinct dose-response relationship even at levels of cumulative exposure below 1 fiber year. Moreover, the study confirms that asbestos is a relevant confounder for MMVF. A causal relationship between exposure to MMVF and mesothelioma could neither be detected nor excluded, as in other studies.

9. Code(s): 6, 9.

Muhle, H. and F. Pott. (2000). "Asbestos as reference material for fibre-induced cancer." Int Arch Occup Environ Health. 73 Suppl S53-9.

The objective of this paper is to review published data on the carcinogenicity of asbestos fibres with regard to the elucidation of a potential risk originating from exposure to man-made vitreous fibres (MMVF). Steps in the comparison of the two fibre classes are characterization of the fibres, pulmonary deposition, biodurability and biopersistence and a review of the cancer risk from asbestos fibres after inhalation in rats and humans. Various dust samples of chrysotile, crocidolite, and amosite were used as reference materials in studies with experimental animals. These fibres are normally thinner and shorter than MMVF. These differences in dimensions cause differences in the deposition in the airways. In addition, significant dissimilarities exist in the deposition pattern between rats and humans. Data from biopersistence studies show that focusing only on fibres longer than 20 microm and using weighted half-time for a characterization of risk may be misleading. Inhalation experiments with rats need fibre exposure concentrations over 100 times higher to match the lung cancer risk of asbestos workers, and about 1,000 times higher to reach the same mesothelioma risk. Also, the striking difference between the low lung burden of amphibole fibres of asbestos workers with mesothelioma and the more than 1,000 times higher lung burden of rats with a low mesothelioma risk demonstrates the low sensitivity of the inhalation test model for the carcinogenic potency even of crocidolite fibres. It can be concluded that the rat inhalation model is also not sensitive enough to predict the cancer risk of other fibre types for humans.

10. Code(s): 6, 9.

Gilmour, P. S., D. M. Brown, P. H. Beswick, W. MacNee, I. Rahman and K. Donaldson. (1997). "Free radical activity of industrial fibers: role of iron in oxidative stress and activation of transcription factors." Environ Health Perspect. 105 Suppl 5 1313-7.

We studied asbestos, vitreous fiber (MMVF10), and refractory ceramic fiber (RCF1) from the Thermal Insulation Manufacturers' Association fiber repository regarding the following: free radical damage to plasmid DNA, iron release, ability to deplete glutathione (GSH), and activate redox-sensitive transcription factors in macrophages. Asbestos had much more free radical activity than any of the man-made vitreous fibers. More Fe3+ was released than Fe2+ and more of both was released at pH 4.5 than at pH 7.2. Release of iron from the different fibers was generally not a good correlate of ability to cause free radical injury to the plasmid DNA. All fiber types caused some degree of oxidative stress, as revealed by depletion of intracellular GSH. Amosite asbestos upregulated nuclear binding of activator protein 1 transcription factor to a greater level than MMVF10 and RCF1; long-fiber amosite was the only fiber to enhance activation of the transcription factor nuclear factor kappa B (NF kappa B). The use of cysteine methyl ester and buthionine sulfoximine to modulate GSH suggested that GSH homeostasis was important in leading to activation of transcription factors. We conclude that the intrinsic free radical activity is the major determinant of transcription factor activation and therefore gene expression in alveolar macrophages. Although this was not related to iron release or ability to deplete macrophage GSH at 4 hr, GSH does play a role in activation of NF kappa B.

11. Code(s): 6, 9.

Everitt, J. I., E. Bermudez, J. B. Mangum and P. C. Ferriola. (1996). "Malignant mesothelioma: a legacy of asbestos that affects the safety evaluation of synthetic vitreous fibers." CIIT Activities; 16(9):1-6 1996.

Since the demonstration in 1960 by J. C. Wagner et al of the association between malignant mesothelioma and exposure to amphibole asbestos fibers, this cancer has become of major interest in experimental carcinogenesis studies. Experimental animals exposed to a number of natural mineral fibers and synthetic vitreous fibers develop this rare malignancy. Research at the Chemical Industry Institute of Toxicology (CIIT) has focused on the changes in mesothelial cells that are induced by fibers. This is a brief overview of work in this area at CIIT. Mesothelial cells express the Wilms' tumor suppressor gene WT-1, and this serves as a useful marker for differentiation of these cells. As regards growth factors, tumor cells differ from normal in that they express transforming growth factor alpha (TGFalpha) whereas normal cells do not, although both express the receptor EGF-R. Tumor cells induced by fiber do not express insulin-like growth factor II, unlike normal cells and spontaneous tumors. Although most studies have concentrated on the rat model, this does differ from human mesothelioma cells in that only the receptor (PDGF-R) for platelet-derived growth factor (PDGF) occurs in normal and neoplastic rat mesothelioma cells; both occur in human cells. There is evidence that oxidant-mediated injury is an important mechanism for fiber-induced disease. The results of rodent inhalation assays in which post-mortem, molten agarose is instilled into the pleural cavities to form casts that contain entrapped fibers are briefly reviewed. The fibers that most rapidly locate to the pleural space are associated with inflammatory changes and mesothelial cell proliferation, the latter especially marked among the parietal pleural mesothelial cell population. Changes in extracellular matrix proteins are discussed next. Nontumorigenic immortalized rat mesothelial cells show abundant levels and organization of fibronectin; this may actually help mediate mineral fiber-cell interactions since fibronectin binds to mineral fibers. Mesotheliomas are invasive but rarely metastatic, and this may relate to the unusual amount and properties of the fibronectin matrix and cytoskeleton. Finally, the subjects of rodent bioassays and future experiments are briefly discussed.

12. Code(s): 6, 11.

Chang, H. Y., C. R. Chen and J. D. Wang. (1999). "Risk assessment of lung cancer and mesothelioma in people living near asbestos-related factories in Taiwan." Archives of Environmental Health; 54 (3). 1999. 194-201.
BIOSIS COPYRIGHT: BIOL ABS. Estimates from environmental risk assessments are criticized by professionals who indicate that inaccuracies occur in exposure assessment, model selection, and determination of the population at risk. In the current study, we tackled the aforementioned issues and estimated the risks of lung cancer and mesothelioma caused by airborne asbestos among individuals who lived near asbestos factories in Taiwan. We conducted 8-h full-period samplings upwind and downwind from each factory, and we used tra elioma models were patterned after the first-exposure-effect models developed by Peto and Finkelstein. The data obtained from phase-contrast microscopy significantly overestimated the risk, compared with transmission-electronic microscopy. The estimates we calculated from adopting the arithmetic mean were approximately 2-fold higher than those we calculated with the geometric mean. There were relatively low concentrations of asbestos in the study areas, thus causing an absence of

13. Code(s): 7.
Oberdorster, G. (2000). "Determinants of the pathogenicity of man-made vitreous fibers (MMVF)." Int Arch Occup Environ Health. 73 Suppl S60-8.
INTRODUCTION AND OBJECTIVES: A number of man-made vitreous fibers (MMVF) have been developed over the years to replace asbestos fibres in its uses as insulating material. Concerns have been raised that these man-made fibers may also pose a significant health hazard when inhaled during their manufacture and application. As will be discussed in this brief overview, dose, dimension and durability of fibrous particles are key parameters with respect to the induction of adverse pulmonary effects, including carcinogenicity as well as non-cancer effects. In particular, fiber biopersistence plays a most important role for pulmonary pathogenicities, and consequently biopersistence receives greatest attention in the search of new fibrous materials. METHODS AND RESULTS: Tests to evaluate fiber biopersistence include the administration of fibers by a short-term inhalation (5 days) or intratracheal instillation into rats. Advantages of the inhalation methodology include the even distribution throughout the lung administered by a physiological process. A disadvantage of this method is the limited respirability of long fibers in the rat whereas they are well respirable by humans. Such long fibers (> 20 microm) have the greatest potential for tumorigenicity and need special consideration in connection with the evaluation of fiber biopersistence. Enrichment of the inhaled aerosol by these long fibers needs to be considered in order to deposit enough of them in the lower respiratory tract of the rat. In contrast, the advantage of the instillation technique is that these long fibers can be delivered to the lung. However, the major disadvantages of intratracheal instillations are the potential of the administered fibers to form clumps and aggregates in the airways and the induction of a major inflammatory response when high-bolus doses are administered. This could influence fiber dissolution in the lungs significantly. CONCLUSIONS: At the same delivered lung dose, a fiber of low biopersistency has the least effect and is, therefore, less likely to induce lung or pleural tumors even under chronic exposure conditions. Respective animal studies with more fibers of different biopersistence have confirmed this general principle. It is very important that, when evaluating and interpreting fiber effects observed in experimental animals, species differences with respect to respirability, lung retention and mechanisms of responses are considered.

14. Code(s): 8, 9.
Lockey, J. E. (1996). "Man-Made Fibers and Nonasbestos Fibrous Silicates." Occupational and Environmental Respiratory Disease, P. Harber, M. B. Schenker and J. R. Balmes, Eds; Mosby-Year Book, Inc., St. Louis, MO, pp 330-344, 101 refs.
A review of the determinants of fiber toxicity and the health effects of exposure to man made fibers and nonasbestos fibrous silicates was presented. The main determinants of fiber toxicity were reported to be dose, fiber size and fiber durability. Fibers of less than 3.5 micrometers (microm) in diameter and 200microm in length were reported to be respirable. Studies under review noted that fibers from 0.25 to 1.5microm in diameter and above 4 to 8microm in length were most carcinogenic, and that fiber toxicity increased with increasing durability. Man made fibers under consideration were of four types. Carbon/graphite (7440440) fibers were reported as variable in their toxicity. Kevlar-para-aramid fibers were reported to provide minimal human risk. Silicon-carbide (409212) fibers were noted to be a potential cause of pulmonary fibrosis. Man made vitreous fibers were described in terms of their manufacturing process, industrial and commercial applications, relevant animal inhalation studies, health effects and relevant mortality studies. Animal and mortality studies were reported to show a possible link between exposure and cancer. Other health effects include skin, eye and airway irritation and pleural plaques. Four types of fibrous silicates were reviewed. Attapulgite (12174117) and sepiolite (63800373) carcinogenesis studies produced variable results. Wollastonite (13983170) studies showed low carcinogenic and fibrogenicpotentials. Zeolite (1318021) animal and human studies showed potential fibrogenicity and carcinogenicity. Vermiculite (1318009), talc (14807966) and metal ore deposits were characterized as minerals with potential fiber contamination with varying levels of carcinogenicity. The author concludes that care should be taken in the workplace to avoid contact with potentially toxic fibers.

15. Code(s): 8, 11.
Ruegger, M. (1996). "[Are artificial mineral fibers harmful to health and unsuitable for asbestos substitute?]." Schweiz Rundsch Med Prax. 85 (33): 961-6.

The increasing knowledge about the carcinogenic properties of asbestos have given rise to an extensive research on possible adverse health effects of alternative materials. Especially man-made mineral fibers (MMMF), i.e. glass fibers, but also glass-, stone- and slag wools turned out to be of unique interest, because they have already been used for several decades for isolation purposes. It is generally accepted that the carcinogenic potential of any fiber is related to its dimension and its biopersistence. Based on series of experiments, it could be demonstrated that only fibers longer than 5 microns, thinner than 3 microns and with a length/diameter ratio of more than 3 are able to reach the periphery of the lung. Excepting the refractory (ceramic) fibers, studies showed that inhalation did not provoke tumors in rodents, whereas the intratracheal, intrapleural and intraperitoneal instillation induced a carcinogenic effect for most kinds of MMMF. Compared to asbestos, MMMF clears out much faster from the lung tissue. Finally, there is no consistent epidemiological evidence for an increased standardized mortality ratio due to malignant tumors of the airways and malignant mesotheliomas in individuals formerly exposed to MMMF. Out of the rather theoretical tumor risk, there is a far more common and itchy skin problem to mention, namely glass-fiber dermatitis, which appears when one is handling without protection thicker and therefore more stinging fibers. In the light of these facts and based on the actual exposure situation, there is no clearcut cancer risk, when one is handling glass fibers and wool; however, the potential risk of exposure to refractory ceramic fibers has to be evaluated with more caution.

16. Code(s): 8, 15.
Hesterberg, T. W. and G. A. Hart. (2001). "Synthetic vitreous fibers: a review of toxicology research and its impact on hazard classification." Crit Rev Toxicol. 31 (1): 1-53.
Because the inhalation of asbestos, a naturally occurring, inorganic fibrous material, is associated with lung fibrosis and thoracic cancers, concerns have been raised about the possible health effects of synthetic vitreous fibers (SVFs). SVFs include a very broad variety of inorganic fibrous materials with an amorphous molecular structure. Traditionally, SVFs have been divided into three subcategories based on composition: fiberglass, mineral wool (rock, stone, and slag wools), and refractory ceramic fiber. For more than 50 years, the toxicologic potential of SVFs has been researched extensively using human epidemiology and a variety of laboratory studies. Here we review the research and its impact on hazard classification and regulation of SVFs. Large, ongoing epidemiology studies of SVF manufacturing workers have provided very little evidence of harmful effects in humans. Several decades of research using rodents exposed by inhalation have confirmed that SVF pulmonary effects are determined by the "Three D's", fiber dose (lung), dimension, and durability. Lung dose over time is determined by fiber deposition and biopersistence in the lung. Deposition is inversely related to fiber diameter. Biopersistence is directly related to fiber length and inversely related to fiber dissolution and fragmentation rates. Inhaled short fibers are cleared from the lung relatively quickly by mobile phagocytic cells, but long fibers persist until they dissolve or fragment. In contrast to asbestos, most of the SVFs tested in rodent inhalation studies cleared rapidly from the lung (were nonbiopersistent) and were innocuous. However, several relativley biopersistent SVFs induced chronic inflammation, lung scarring (fibrosis), and thoracic neoplasms. Thus, biopersistence of fibers is now generally recognized as a key determinant of the toxicologic potential of SVFs. In vitro dissolution of fibers in simulated extracellular fluid correlates fairly well with fiber biopersistence in the lung and pulmonary toxicity, but several exceptions suggest that biopersistence involves more than dissolution rate. Research demonstrating the relationship between biopersistence and SVF toxicity has provided a scientific basis for hazard classification and regulation of SVFs. For a nonhazardous classification, legislation recently passed by the European Union requires a respirable insulation wool to have a low lung-biopersistence or be noncarcinogenic in laboratory rats. U.S. fiberglass and mineral wool industries and the Occupational Health and Safety Administration (OSHA) have formed a voluntary Health and Safety Partnership Program (HSPP) that include: a voluntary permissible exposure level (PEL) in the workplace of 1 fiber/cc, a respiratory protection program for specified tasks, continued workplace air monitoring, and, where possible, the development of fiber formulations that do not persist in the lung. RCF manufacturers have implemented a Product Stewardship Program that includes: a recommended exposure guideline of 0.5 fibers/cc; a 5-year workplace air monitoring program; and research into the development of high-temperature-resistant, biosoluble fibers.

17. Code(s): 11.
Breysse, P. N., P. S. Lees, B. C. Rooney, B. R. McArthur, M. E. Miller and C. Robbins. (2001). "End-user exposures to synthetic vitreous fibers: II. Fabrication and installation fabrication of commercial products." Appl Occup Environ Hyg. 16 (4): 464-70.
This article summarizes the results of exposure monitoring conducted during the installation and fabrication of commercial synthetic vitreous fiber (SVF) products. Included in this investigation were fiberglass duct insulation and construction applications (duct board, duct liner, and duct wrap), pipe and vessel insulation, batt insulation for prefabricated homes, and general fiberglass products. Commercial mineral wool products sampled as a part of this investigation included ceiling tiles, building safing, and loose insulation for prefabricated homes. A total of 520 valid air samples were collected as a part of this investigation and were analyzed using gravimetric, phase contrast microscopy (PCM), or scanning electron microscopy (SEM). Airborne fiber- size distributions were also determined for a subset of samples collected for SEM analysis. As a result of the task-based sampling strategy used in this study, sample times reflect exposures over the time the person was actually engaged in SVF-related work activities, and exposure results are therefore presented as task-length averages (TLAs). Thirty-five total dust samples were collected as a part of this investigation,

resulting in 14 TLAs ranging from 0.3 to 7.6 mg/m3. A total of 125 PCM-based TLAs were collected, with the mean TLA time for all product and occupation categories ranging from 277 to 443 minutes. The mean PCM-based TLAs for all product/occupations were below 1.0 f/cm3, ranging from 0.04 to 0.68 f/cm3. A total of 116 SEM TLAs were determined. Average SEM-based TLA concentrations were slightly lower than the PCM-based estimates and ranged from <0.01 to 0.16 f/cm3. The geometric mean fiber diameters for commercial products and occupations sampled as a part of the investigation ranged from 0.8 microm to 1.9 microm. Geometric mean fiber length varied by a factor of approximately three, ranging from 9.5 microm to 29.5 microm.

18. Code(s): 11.
Carter, C. M., C. W. Axten, C. D. Byers, G. R. Chase, A. R. Koenig, J. W. Reynolds and K. D. Rosinski. (1999). "Indoor airborne fiber levels of MMVF in residential and commercial buildings." Am Ind Hyg Assoc J. 60 (6): 794-800.
Man-made vitreous fibers (MMVF) have been used widely in commercial and residential buildings for over 50 years. Concerns have been expressed since the late 1960s that MMVF products may erode and contribute to fiber levels in the indoor environment. This cooperative investigation was undertaken to quantify indoor respirable fiber levels by phase contrast optical microscopy (PCOM) and to differentiate between fiber types using scanning electron microscopy with energy-dispersive X-ray microanalysis (SEM-EDX). A total of 205 stationary samples were collected using standard industrial hygiene methods in 51 residential and commercial buildings. Twenty-one simultaneous outdoor samples were collected at 19 buildings. All samples were analyzed by PCOM following the NIOSH 7400 Fiber method, "B" counting rules, and 50 randomly selected samples were analyzed by SEM-EDX. The PCOM mean value for all respirable fiber levels was 0.008 f/cc with a median value of 0.007 f/cc and a maximum value of 0.029 f/cc. Ninety-seven percent of the respirable fibers identified by SEM-EDX were determined to be organic. MMVF were detected on only two samples. Airborne fiber levels were very low and the respirable fibers present were primarily organic. The inorganic fiber levels determined by SEM-EDX which included MMVF were less than 0.0001 f/cc.

19. Code(s): 11.
van Orden, D. R., R. J. Lee, K. M. Bishop, D. Kahane and R. Morse. (1995). "Evaluation of ambient asbestos concentrations in buildings following the Loma Prieta earthquake." Regul Toxicol Pharmacol. 21 (1): 117-22.
On October 17, 1989, an earthquake struck central, coastal California including San Francisco and the Bay Area, damaging many buildings. Because of concern over the possible exposure to asbestos in the damaged buildings, building owners/managers hired several Bay Area industrial hygiene firms to collect air samples in suspect buildings. RJ Lee Group analyzed a total of 419 air samples from 55 buildings (25 school, 3 university, 20 commercial, 5 public, and 2 residential buildings) using transmission electron microscopy and has compiled the results. The data from each building were averaged and grouped accordingly into three classifications: indoor buildings, buildings with asbestos abatement in progress at the time of the earthquake, and buildings where sampling was performed to monitor clean-up of debris. Several buildings were sampled on more than 1 day. The results indicate that asbestos levels differed little from outdoor levels, even immediately after the earthquake. Exceptions to this were samples collected in the vicinity of debris clean-up and in buildings undergoing abatement which were higher than the indoor or outdoor samples. However, these samples generally had concentrations below the AHERA clearance levels and all were well below the OSHA action limit.

20. Code(s): 14, 15.
Morgan, A. (1995). "Deposition of Inhaled Asbestos and Man-Made Mineral Fibres in the Respiratory Tract." Annals of Occupational Hygiene, Vol. 39, No. 5, pages 747-758, 40 references, 1995.
Studies on the respiratory tract deposition of inhaled asbestos (1332214) and man made mineral fibers (MMMF) were reviewed and discussed. Fiber diameter has been found to play a large role in the deposition of fibers in rat lungs. Several studies investigated regional deposition within the respiratory tract, showing a trend towards an increase of fiber deposition with a corresponding increase in aerodynamic diameter (Dae). While fiber length was also determined to be of importance, diameter was the stronger factor. Fibers must have a Dae of less than 3 micrometers to be deposited in the alveolar region. The physiological function of the respiratory system served to preferentially allow passage of long thin fibers, which have been found in the deep lung in proportions far greater than their numbers in the source cloud. The author suggests two areas for further research on the deposition and translocation of MMMF: investigate what factors predispose some fibers to be transferred to the interstitium and/or to pulmonary lymphatics following deposition and predispose others to remain free; and determinations of the validity of intratracheal instillation for toxicity studies by comparing the changes in fibers following instillation and inhalation.

21. Code(s): 15.
McConnell, E. E. (2000). "A science-based paradigm for the classification of synthetic vitreous fibers." Regul Toxicol Pharmacol. 32 (1): 14-21.
Synthetic vitreous fibers (SVFs) are a broad class of inorganic vitreous silicates used in a large number of applications including thermal and acoustical insulation and filtration. Historically, they have been grouped into somewhat artificial broad categories, e.g., glass, rock (stone), slag, or ceramic fibers based on the origin of the raw materials or the manufacturing process used to produce them.

In turn, these broad categories have been used to classify SVFs according to their potential health effects, e.g., the International Agency for Research on Cancer and International Programme for Chemical Safety in 1988, based on the available health information at that time. During the past 10-15 years extensive new information has been developed on the health aspects of these fibers in humans, in experimental animals, and with in vitro test systems. Various chronic inhalation studies and intraperitoneal injection studies in rodents have clearly shown that within a given category of SVFs there can be a vast diversity of biological responses due to the different fiber compositions within that category. This information has been further buttressed by an in-depth knowledge of differences in the biopersistence of the various types of fibers in the lung after short-term exposure and their in vitro dissolution rates in fluids that mimic those found in the lung. This evolving body of information, which compliments and explains the results of chronic animal studies clearly show that these "broad" categories are somewhat archaic, oversimplistic, and do not represent current science. This new understanding of the relation between fiber composition, solubility, and biological activity requires a new classification system to more accurately reflect the potential health consequences of exposure to these materials. It is proposed that a new classification system be developed based on the results of short-term in vivo in combination with in vitro solubility studies. Indeed, the European Union has incorporated some of this knowledge, e.g., persistence in the lung into its recent Directive on fiber classification.